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FACTORS INFLUENCING THE AURICULAR MURMUR AND THE INTENSITY OF THE FIRST HEART SOUND

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STUDIES of cases of mitral stenosis in which there were varying degrees of heart block have clearly demonstrated that the presystolic murmur of mitral stenosis is produced by contraction of the auricle.[1, 2, 3] More recently it has been appreciated that presystolic gallop rhythm and certain split heart sounds also result from sound waves initiated by auricular contraction.[4, 5] The relation of the auricular contraction to the intensity of the first heart sound has been investigated by many observers.[6, 7, 8] There has been no unanimity of opinion, however, as to the mechanism by which the auricular contraction modifies the intensity of the first sound. This study is reported for the purpose of emphasizing: (1) the effect of the degree of ventricular filling on the intensity of the sound produced by the auricular contraction; (2) the relative effect on the intensity of the first heart sound of (a) the time of auricular contraction and (b) the degree of ventricular filling.

METHOD

The Cambridge stethograph and the Hindle electrocardiograph were used to record the heart sounds and the electrocardiogram simultaneously. The stethograph consists of three main parts, namely, a large bell microphone that provides a 300 to 400 per cent amplification of sounds in the range between 75 and 550 cycles per second; a vacuum tube amplifier; and a recorder consisting of light source, camera, and galvanometer. The heart sounds were recorded from the apex with the subject in the recumbent position. Lead II was always used for the simultaneously recorded electrocardiogram.

CASE 1.—N. S., a 57-year-old, white, single seamstress, entered the hospital Nov. 4, 1938, with a history of Adams-Stokes attacks for three weeks preceding admission. There was no past history of rheumatic fever, chorea, dyspnea, or angina. In the physical examination the points of interest were confined to the cardiovascular system. The heart was not enlarged. The first sound at the apex was

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accentuated; there were a blowing systolic murmur of moderate intensity, and a presystolic murmur, both of which were maximal at the apex. The heart rate was 80 per minute, and the beating was regular. The blood pressure was 130/60. The peripheral vessels showed moderate thickening. The eye grounds were negative. The clinical impression was sclerosis of the coronary arteries with varying degrees of block, and inactive rheumatic heart disease with a minor degree of mitral stenosis.

While the patient was in the hospital the rhythm of the heart varied from normal to complete block. During periods of 2 to 1 heart block, in addition to

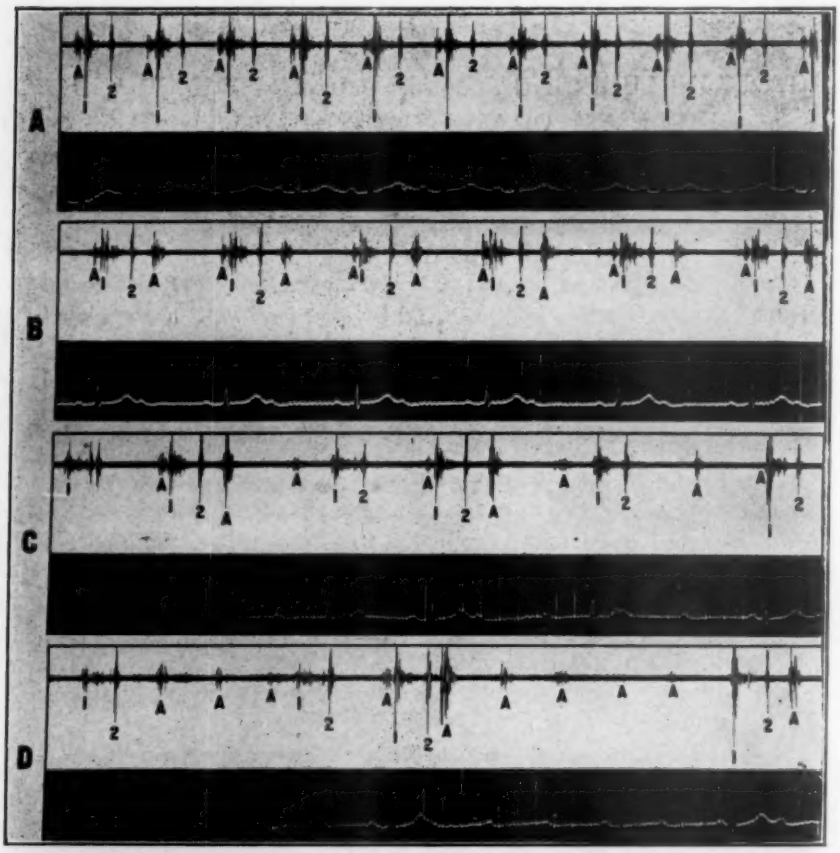

Fig. 1.—Simultaneously recorded electrocardiograms and phonocardiograms in Case 1. Bell microphone placed just inside apex. *A*, auricular murmur; *1*, first heart sound; *2*, second heart sound.

In this and the following figures, unless otherwise stated, the various tracings were taken at different times.

A, Partial heart block; *B*, 2 to 1 heart block; *C*, Complete heart block; *D*, Periods of ventricular standstill.

the presystolic murmur, a second murmur was audible a short time after the second heart sound. This new murmur was usually louder than the presystolic murmur, but differed from it in no other way. With 3 to 1 block two distinct murmurs were audible in addition to the presystolic murmur; the early diastolic murmur was loud, the mid-diastolic murmur faint, and the presystolic murmur barely audible. In periods of complete block, striking differences in the intensity of the first heart sound were noted in certain cardiac cycles, in addition to the

auricular murmurs of varying intensity. At the beginning of the more prolonged periods of ventricular standstill, three or four auricular murmurs, each fainter than the preceding one, were audible. During the remainder of these periods no sounds were audible, although the electrocardiogram showed that the auricles were contracting rhythmically.

Comment.—Simultaneous phonocardiographic and electrocardiographic tracings revealed several facts of interest. Fig. 1 *A* shows partial heart block with a P-R interval of 0.22 second and a rate of 80 per

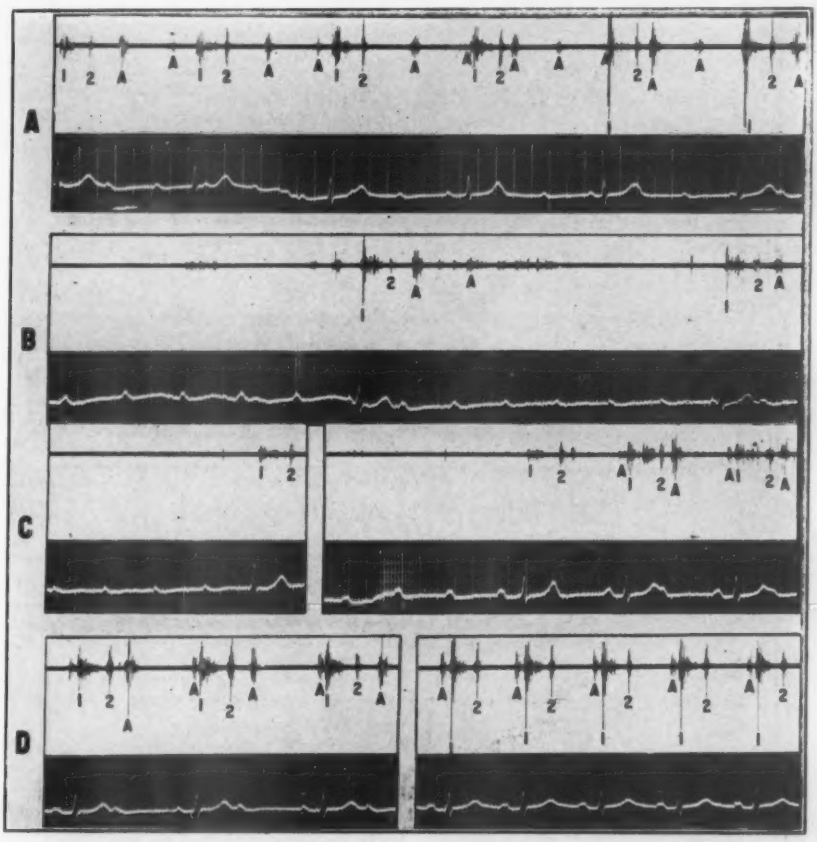

Fig. 2.—Simultaneously recorded electrocardiograms and phonocardiograms in Case 1. Bell microphone placed just inside apex.
A, Complete heart block. The first sounds in the last two beats are accentuated by the auricular contraction. *B* and *C*. Long periods of ventricular standstill. A continuous record with strips omitted between *B* and *C* and after the first ventricular beat in *C*. The first ventricular contraction in *B* and the first and second ventricular contractions in *C* follow 8-second periods of ventricular standstill. *D*, Both 2 to 1 heart block and normal rhythm. A continuous record with a few complexes omitted between the first and second portions.

minute. The presystolic murmur is readily visible. Fig. 1 *B* is a tracing of 2 to 1 heart block with an auricular rate of 84, and a ventricular rate of 42, per minute. When the auricle contracts early in diastole a murmur is produced which is louder than the presystolic murmur. Tracings *C* and *D* show complete block and periods of ventricular standstill. The

auricular rate is about 85. Again, the more closely the auricular contraction follows the second sound, the louder is the murmur produced. This is strikingly shown in the longer periods of ventricular standstill. The fifth auricular beat is barely visible on the sound tracing, and was inaudible.

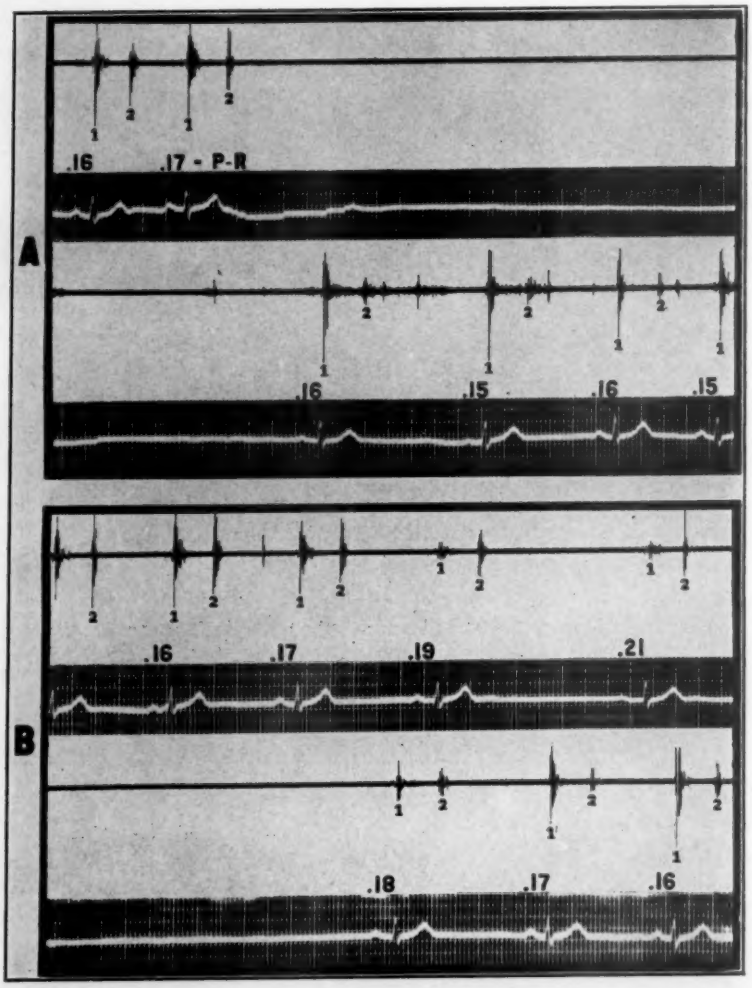

Fig. 3.—Simultaneously recorded electrocardiograms and phonocardiograms in Case 2.
A, A 5-second period of cardiac standstill without change in the P-R interval. The intensity of the first heart sound is not altered. *B*, Increase in P-R interval and short period of cardiac standstill. As the P-R interval is lengthened, the first heart sound decreases in intensity.

Fig. 2 *A* shows the effect of different P-R intervals on the intensity of the first heart sound. In this case the sound is increased in intensity with P-R intervals of 0.18 to 0.04 second. With P-R intervals outside these limits the auricular contraction has no measurable effect on the first heart sound. Tracings *B* and *C* are from the same record. In *B*

the auricles have ceased making any recordable vibrations. Nevertheless, the first heart sound is accentuated by the preceding auricular contraction. Note that the P-R intervals are short, 0.1 and 0.08 second, respectively. In *C*, after long periods of ventricular standstill (15 blocked auricular beats), the first sounds of the initial contractions are very weak, and are widely separated from the auricular beats. Fig. 2 *D* is a continuous tracing illustrating the effect of the ventricular rate on the intensity of the first heart sound. The P-R intervals are the same in the two parts of the tracing, but at a ventricular rate of 43, with a 2 to 1 block, the first sound is much fainter than at a rate of 71.

CASE 2.—R. F., a 65-year-old, white, single laborer, entered the hospital Nov. 28, 1938, complaining of attacks of syncope over a period of two years. Examination disclosed that pressure on the left carotid sinus produced cardiac standstill and syncope. Except for this finding and a moderate degree of arteriosclerosis, physical examination was negative.

Comment.—Fig. 3 shows the effect produced by the application of pressure over the carotid sinus. In tracing *A* the first heart sound is not affected by the 5-second period of cardiac standstill. The P-R interval of the initial beat after the period of cardiac standstill is the same as it was in the period preceding the application of pressure over the carotid sinus. In *B* the first sound becomes fainter as the P-R interval is lengthened, regardless of the ventricular rate. In the initial beat after the period of cardiac standstill, the P-R interval is slightly longer than usual and the first heart sound somewhat fainter. In this subject an increase in the P-R interval from 0.17 to 0.18 second usually produced a decrease in the intensity of the first heart sound; an increase from 0.17 to 0.19 second always produced a marked decrease.

DISCUSSION

Auricular Murmur.—Interest in the sounds produced by auricular contraction was first aroused by study of the presystolic murmur of mitral stenosis. Galabin,[1] in 1875, showed by graphic methods that this murmur was related to the auricular contraction. In 1909, Cohn[2] published tracings obtained from a patient with mitral stenosis and 2 to 1 heart block. These showed that at the time of the auricular contraction there was always a murmur, presystolic in time when the rhythm was normal, which occurred by itself when the ventricle did not contract. Lewis,[3] in a more extensive study, in 1913, showed conclusively that the presystolic murmur was caused by the auricular contraction. He demonstrated that it was not really a crescendo murmur, but sounded so because of its proximity to the accentuated first sound. Bramwell,[9] in a study of heart block and mitral stenosis, showed that there was a striking variation in the intensity of the auricular murmur in different cycles. When the auricular contraction occurred early in diastole the murmur was loud, but when it occurred at the end of a prolonged diastole it was

often so faint that it failed to reach the threshold of audibility. He gave the following explanation for this variation. When the auricular contraction immediately follows the second sound, a loud noise is produced because the blood is forced rapidly into the empty ventricle. Each succeeding auricular beat produces less sound because the engorged ventricle accepts less blood each time. Cossio[10] also states that the presystolic murmur of mitral stenosis may be absent after long diastoles because of the inability of the auricle to inject blood into an overdistended ventricle.

In more recent years attention has been centered on the normal auricular sounds. These have been recorded both from the precordium and from the esophagus. Cossio and Fongi[4] state that the auricular sound is formed by two groups of small oscillations, appearing a few hundredths of a second apart. With the receiver in the esophagus, the initial portion of the sound is more constant and predominates in the record, but when the auricular sound is recorded from the precordium, it is the second part of the sound that predominates. Wolferth and Margolies,[6] in a study of seven cases of heart block, noticed that the murmur produced by auricular contractions falling early in diastole was louder and more prolonged than that produced by contractions late in diastole. They also concluded, as did Bramwell[9] in his study of mitral stenosis, that the auricular murmur which they recorded was produced by the passage of blood from auricle to ventricle, rather than by the contraction of the auricular muscle itself. They based their conclusions on the time relation between the P wave in the electrocardiogram and the auricular murmur, and on the fact that the maximal auricular murmur occurred early in diastole, when the contraction would have the maximal effect on blood flow.

The tracings from Case 1 show the relation between the P wave and the auricular murmur. This murmur occurred 0.14 second after the beginning of the P wave, while the first sound started from 0.02 to 0.04 second after the beginning of the R wave. The degree of ventricular filling played the decisive role in determining the intensity of the murmur produced by the auricular contraction. As this would be true regardless of whether the auricular murmur was caused by a slight degree of mitral stenosis or by an abnormally vigorous auricular contraction, it is not possible to make an etiologic diagnosis from the tracings. The accentuated first sound with partial heart block and a ventricular rate of 80 beats per minute is, however, suggestive of mitral stenosis. During the discussion of the cause of the accentuated first sound in certain cycles during complete block, additional evidence will be presented to show that the auricular murmur in Case 1 is produced only when blood enters the ventricles, and that it is not produced by contraction of the auricular muscle itself.

First Heart Sound.—Textbooks of physiology and of physical diagnosis usually state that there are two factors in the production of the

first heart sound: (1) the sudden closing of the mitral and tricuspid valves; and (2) the contraction of the heart muscle. Dock,[11] in 1933, on the basis of experiments on the exposed hearts of dogs, stated that there is no muscular element in the first heart sound, and that ventricular contraction produces no audible vibrations in either empty or full hearts if tensing of the auriculoventricular valves is prevented. He stated also that if the valves are closed and the intraventricular pressure is about as high as the pressure within the auricle, ventricular contraction causes only a faint first sound; if the valves are slack and displaced toward the ventricles by the rush of blood through them, ventricular contraction produces a loud first sound. The evidence obtained in our two cases lends support to Dock's conclusions.

In Case 1 the first heart sound was intensified whenever auricular electrical systole began from 0.18 second to 0.04 second before ventricular electrical systole. This accentuation of the first heart sound by the auricular contraction has been described by many observers.[6, 7, 8] Some authors[6, 12] have stated that a moderate increase in intensity occurs regularly in certain cases when ventricular electrical systole precedes auricular electrical systole by a few hundredths of a second. Careful analysis of a large series of tracings obtained in Case 1 failed to reveal any accentuation of the first sound unless the P wave preceded the R wave. An explanation for this apparent discrepancy has been furnished by the work of Wolferth and Margolies[13] on the influence of varying P-R intervals on split first heart sounds. In two cases of complete heart block the first portion of the split heart sound was not accentuated unless the P-R interval exceeded 0.03 and 0.05 second, respectively. In these cases, however, the second portion of the first heart sound was accentuated when the P wave was buried in the QRS complex. Wolferth and Margolies believed that in these cases the contractions of the right and left ventricles were not perfectly synchronized. The auricular contraction, therefore, could still influence the portion of the first sound developed from one side of the heart, although contraction of the opposite ventricle had already closed one set of valves and produced the first portion of the first heart sound.

There have been two principal explanations for the accentuation of the first heart sound by the auricular contraction: (1) It is the result of the summation of the auricular and ventricular sound waves[14]; (2) it is the result of a change in the position of the auriculoventricular valves at the beginning of ventricular contraction.[6, 11] The fact that, in Case 1, accentuation of the first sound persisted when the P-R interval was shortened after long periods of ventricular standstill, and after the auricular contractions had ceased to make any sound waves, indicates that the accentuated first sound was not the summation of the normal auricular and ventricular sound waves. The best explanation of the accentuation of the first sound is that it results from an increase in intra-auricular

pressure sufficiently great to produce slackening of the auriculoventricular valves. The ventricular contraction causes sudden tightening of the previously slack valve structures and produces an intensified sound. The possibility exists that with a long P-R interval blood may flow backward, from ventricle to auricle, and produce a weak first sound because the ventricle contains less blood than normally. The fact that the auricular murmur disappears during the longer periods of ventricular standstill indicates that the ventricles are too full to accept more blood, which renders this explanation untenable. Likewise, accentuation of the first sound cannot result from an increase in the amount of blood in the ventricles brought about by the immediately preceding auricular contraction, because accentuation occurs with short P-R intervals even when the auricular contractions have ceased passing much blood into the ventricles.

Accentuation of the first heart sound occurred when the auricular murmur (not the P wave) started from 0.07 second before the beginning of the first sound to 0.07 second after the beginning of the first sound. The fact that the first sound may be accentuated, even when the auricular murmur is prevented by the ventricular contraction, indicates that the auricular pressure has already risen before the auricular murmur is produced, and that the murmur does not result from the contraction of the auricular muscle itself. The time relation suggests that the rise in intra-auricular pressure with displacement of the auriculoventricular valves toward the ventricle is the important factor in the production of the accentuated first heart sound, and that little flow of blood from auricle to ventricle is necessary to produce accentuation of the first heart sound. This is corroborated by the fact that the first sound is accentuated when the P-R interval is short and the auricular contraction is no longer passing enough blood into the ventricle to produce a murmur.

A second major factor modifying the intensity of the first heart sound is the ventricular rate. This is best shown in Fig. 2 *D*. The first portion of the tracing shows 2 to 1 block with a P-R interval of 0.2 second; the second, normal rhythm with the same P-R interval. With the more rapid rate and a shorter time for ventricular filling, the first sound is much louder than with the slower rate. The louder first sound with the more rapid rate is the result of the shorter ventricular diastole rather than of a change in the auricular beat, since the P-R intervals are the same at both rates, and since in this particular subject studies during periods of complete block have shown that the auricular contraction has no effect on the first sound when the P-R interval is as long as 0.2 second. Likewise, after prolonged periods of ventricular standstill the first sound is uniformly weak unless the auricular contraction immediately precedes it, even though, as indicated by the absence of the auricular murmur, the ventricle is still full of blood. The longer the period of ventricular diastole, the more time the auriculoventricular valves have to float back to a position of closure. Thus, when the ventricle contracts most of the

slack has already been removed from the valves and a less intense sound is produced. If contraction of the ventricular muscle played an important part in the production of the first heart sound, the sound should be intensified in 2 to 1 block, for the longer diastole and the two auricular contractions allow the ventricle to fill more completely.

Case 2 offered an opportunity to ascertain whether the auricular contraction or the ventricular rate is the predominant factor in producing a first heart sound of normal intensity. Pressure on the carotid sinus produced periods of cardiac standstill, some of which were terminated by beats with a normal P-R interval, others by beats with a prolonged P-R interval. Following periods of cardiac standstill lasting as long as 5 seconds, the first sound of the initial beat was of normal intensity when the P-R interval was unchanged; it was uniformly greatly decreased in intensity when the P-R interval was prolonged beyond 0.18 second. Thus, in both of our cases, when the P-R interval was short enough to influence the character of the first sound, prolongation of ventricular diastole had little effect on the intensity of the first sound. In Case 1, when the P-R interval was sufficiently long not to be influenced by the auricular contraction, the first sound became progressively weaker as the duration of diastole increased.

Wolferth and Margolies[6] have made the suggestion that the duration of the auriculoventricular interval within the normal range may be of importance in determining the character of the first heart sound. Keith,[15] in a study of rheumatic heart disease in children, found that the P-R interval could be predicted with a fair degree of accuracy from the intensity of the first heart sound. The observations in Case 2 indicate that under certain conditions an increase in the P-R interval may be recognized clinically if sufficient attention is paid to the intensity of the first heart sound. This point has proved to be of practical value in the diagnosis of first degree heart block.

SUMMARY AND CONCLUSIONS

1. Two subjects, one with an auricular murmur and varying degrees of heart block, the other with attacks of partial heart block and cardiac standstill induced by pressure over the carotid sinus, were studied by means of simultaneously recorded electrocardiograms and phonocardiograms.

2. The auricular murmur recorded from the precordium was not the result of sound waves produced by the contraction of the auricular muscle itself. It was produced only when blood entered the ventricle.

3. The intensity of the auricular murmur in a given case depends on the difference between the auricular and ventricular pressures at the time of the auricular contraction. Early in diastole this difference is marked and the murmur loud; in the latter portion of long diastolic pauses the difference is much less, and the murmur either faint or absent.

4. The first heart sound in Case 1 was accentuated during periods of complete block when the P-R interval ranged between 0.18 and 0.04 second. Evidence is presented to show that this accentuation was the result of displacement of the auriculoventricular valves toward the ventricle by the auricular contraction.

5. The first heart sound became progressively weaker, as ventricular diastole increased in duration, when the P-R interval was too long for the auricular contraction to affect the first sound.

6. When the P-R interval was short enough for the auricular contraction to affect the intensity of the first sound, the auricular contraction played the dominant rôle in determining the intensity, and lengthening of ventricular diastole had no effect.

7. These observations support the conclusion that in normal hearts the position of the auriculoventricular valves at the beginning of ventricular contraction is the primary factor in determining the character of the first heart sound.

8. Variation in the length of the P-R interval, within normal limits, may produce striking alterations in the intensity of the first heart sound.

The authors wish to express their sincere appreciation to Dr. Soma Weiss for his many helpful suggestions and guidance in this work, and to Miss Sophia M. Simmons for technical assistance.

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THE EFFECT OF POSTURE ON THE FORM OF PRECORDIAL LEADS OF THE ELECTROCARDIOGRAM

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PRECORDIAL electrocardiographic leads have come into general use since Wolferth and Wood[1] first employed them in the diagnosis of acute coronary occlusion. With the introduction of the new technique, it was to be expected that the use of many different precordial derivations by different workers would lead to confusion. In order to clarify this situation, the American Heart Association has recently recommended that precordial leads be standardized.[2] Although the optimum location of the exploring electrodes has been widely investigated, out of which has grown a measure of standardization, very little consideration has been given to alterations that occur in precordial leads with change in the position of the patient.

Numerous observations have been made of the changes occurring in the three standard leads of the electrocardiogram when the patient assumes different positions,[3-9] especially with regard to the shift of the "electrical axis" of the heart. Chest leads have been recorded, however, in only a few of these investigations. Although Katz and Robinow[10] recorded electrocardiograms, including precordial leads, with subjects in eight different positions, they discussed only the changes which occurred in the three standard leads. Sigler[11] made chest leads with patients in the supine, sitting, and standing positions, but his paper deals chiefly with the changes found in the three standard leads.

The observations now being reported were made in an attempt to clarify the variations that might be expected in precordial leads when the posture of the subject is changed.

METHODS

Sixteen patients were studied. Four patients (Cases 1, 2, 3, and 4) exhibited normal hearts; in Case 5 there was pneumothorax on the right side with displacement of the heart to the left; three patients (Cases 6, 7, and 8) suffered from rheumatic heart disease with mitral stenosis and insufficiency and predominant enlargement of the right ventricle, and four patients (Cases 9, 10, 11, and 12) from rheumatic lesions of both the aortic and the mitral valves but with enlargement of the left ventricle predominating; in Case 13 there were emphysema and enlargement of the right ventricle; one patient (Case 14) suffered from arteriosclerotic heart disease without cardiac enlargement; two patients (Cases 15 and 16) exhibited the syndrome of chronic constrictive pericarditis. In Cases 6, 7, 10, 11, 14, and 15, chest leads were taken both before and after therapeutic doses of digitalis had been given, in order to observe the effect of this drug on the form of the

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chest leads. In all, forty-one sets of chest leads were made. Two or more observations were recorded on eight of the patients. On each of the remaining eight patients only one set of records was obtained. All observations were made with the patients in a basal metabolic state.

In addition to the three standard leads, three precordial derivations were recorded. The indifferent electrode was placed in the left interscapular region.[1] In one of the three chest leads the precordial electrode was placed in the midsternal line at the level of the fourth intercostal space (Chest Lead A); in the second chest lead the electrode was placed halfway between the first point and the apex (Chest Lead B); in the third, the electrode was placed at the apex (Chest Lead C). The skin was marked, and care was exercised to apply the electrodes at the same areas when subsequent records were taken. Lead plates measuring 6 x 4.5 cm. were used for electrodes. Each chest lead was taken with the patient in each of three positions, namely, supine, sitting up in bed at an angle of 90 degrees, and lying on the left side. All records were made with the right arm wire connected to the precordial electrode, and the left arm wire to the left interscapular electrode.[1] In order, however, to promote and facilitate uniformity in discussing chest leads, the films were printed so that the direction of the complexes corresponds to that in the leads recommended by the American Heart Association.[2]

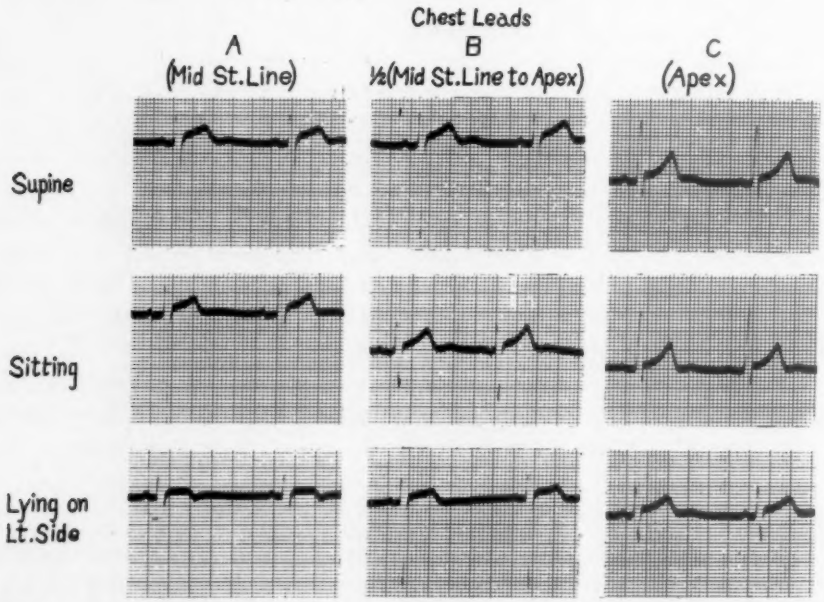

Fig. 1.—In this figure, as well as in Figs. 2 and 3, reproductions of the three chest leads (A, B, and C) are shown. Each of the leads was taken in each of three positions (supine, sitting, and lying on the left side, respectively). In Chest Lead A the exploring electrode was on the midsternal line at the level of the fourth intercostal space. In Chest Lead B the electrode was halfway between this point and the apex. In Chest Lead C the exploring electrode was at the apex. All tracings were taken with the right arm wire connected to the precordial electrode, and the left arm wire to the left interscapular electrode[1]. In order to promote and facilitate uniformity, however, the films were printed so that the direction of the complexes corresponds to that in the leads recommended by the American Heart Association[2]. Divisions of the ordinates equal 10^{-4} volt. Divisions of the abscissae equal 0.04 second. The electrocardiograms in all figures are reduced to half of their original size. In this figure the chest leads of E. K. (Case 1), taken April 8, 1935, are reproduced. The records in this case serve to illustrate the change that occurred in the chest leads of a normal subject as his position was changed from supine, to sitting, to lying on the left side. Decrease in the amplitude of the T waves was the most constant change, but there was also a decrease in the amplitude of the R waves. The S waves showed no constant change.

OBSERVATIONS

The results are recorded in Table I.

(1) Changes in subjects whose hearts were normal.—In these cases (Cases 1 to 4, inclusive), the most frequent change was a decrease in the amplitude of the T wave as the subject changed from the supine position to sitting, and from sitting to lying on the left side (Fig. 1). In Case 2 the T wave became diphasic in leads A and B when the subject lay on the left side, although it had been upright in the other two positions. This also occurred in lead A of the first record (April 8, 1935) taken in Case 1. The amplitude of the R wave decreased as the subject's position changed from supine, to sitting, to lying on the left side. The R and T waves varied concordantly in most instances. There was a change in the amplitude of the S wave in most cases, but it was not constant.

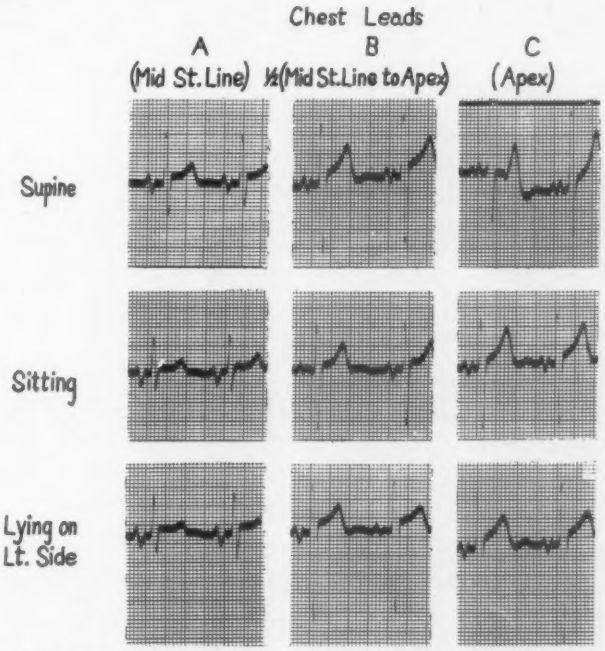

Fig. 2.—In this figure the chest leads of F. S. (Case 6), taken April 13, 1935, are reproduced. The records in this case serve to illustrate the change that occurred in the chest leads of patients exhibiting right ventricular preponderance. There was a decrease in the amplitude of the R waves and T waves as the patient's position was changed from supine, to sitting, to lying on the left side. The S waves showed no constant change.

(2) Changes in a subject with pneumothorax on the right side and displacement of the heart to the left.—In this patient (Case 5), the electrocardiogram showed no abnormal deviation of the electrical axis. Only slight changes were found in the chest leads taken in different positions. The heart was probably relatively fixed in its position as well as displaced by the pneumothorax.

(3) Changes in patients with rheumatic lesions of the mitral valve and preponderant enlargement of the right ventricle.—In these cases

TABLE

CHANGES IN THE

WITH CHANGE

CASE NO.	NAME	AGE	SEX	HOSPITAL NUMBER	DATE	AXIS DEVIATION	CHEST LEAD—A (CHEST ELECTRODE ON MIDSTERNAL LINE)								
							SUPINE			SITTING			LYING ON LEFT SIDE		
							R	S	T	R	S	T	R	S	T
1.	E. K.	24	♂	7924	4/ 8/35	0*	+↑	−	+	+	−↓‡	+	+↓	−↑	±↓
					4/ 9/35	0	+	−	+	+	−	+↓	+↓	−	+
					4/10/35	0	+	−	+	+↑	−↓	+↑	+↓	−↑	+↓
2.	H. C.	21	♂	85691	2/15/35	0	+	−	+	+↑	−↓	+↑	+↓	−↑	±↓
3.	J. MacL.	28	♂	107863	10/ 2/35	0	+	−	+	+↓	−	+	+↑	−↓	+↓
4.	J. G.	46	♂	65699	11/ 2/34	0	+	−	+	+↓	−↑	+↓	+↑	−↓	+↑
5.	T. C.	32	♂	70382	11/23/34	0	+	−	+	+	−↓	+	+↑	−↓	+↑
					11/30/34	0	+	−	+	+↓	−↓	+↓	+↓	−↑	+
					1/12/35	0	+	−	+	+↓	−↓	+	+↓	−	+↓
6.	F. S.	24	♂	89187	4/13/35	R	+	−	∓	+↓	−↑	+	+↑	−↓	+↓
					4/15/35	R	+	−	∓	+↑	−↓	∓	+↓	−↑	∓↓
					4/16/35	R	+	−	∓	+	−↑	∓↑	+↑	−↑	∓↓
					4/19/35	R	+	−	+	+↓	−↑	∓↓	+↑	−↓	∓↑
7.	A. G.	23	♂	79037	11/12/34	0	+	−	+	+↑	−	+↑	+	−	+
					11/14/34	0	+	−	+	+↑	−↑	+	+↓	−↓	+
					11/16/34	0	+	−	+	+↓	−↑	+↓	+↓	−	+↓
					11/17/34	0	+	−	+	+↓	−↑	+↓	+↑	−	+↓
					11/27/34	0	+	−	+	+↑	−↓	+↑	+↓	−	+↓
					1/10/35	0	+	−	+	+↓	−↑	+↓	+↓	−↑	+↓
					3/28/35	0	+	−	+	+	−↑	+↓	+↑	−↑	+↑
8.	F. M.	32	♂	66492	11/ 1/34	0	+	−	−	+↑	−↓	+↑	+↓	−↑	+↓
9.	H. W.	39	♂	44299	1/ 4/35	L	+	−	+	+↓	−↑	+↓	+	−↑	+↓
10.	E. P.	21	♂	14535	11/ 8/34	L	+	−	+	+↑	−↑	+↑	+↓	−↑	+↓
					11/10/34	L	+	−	+	+↓	−	+↓	+↓	−	+↓
					11/13/34	L	+	−	+	+	−↑	+↓	+	−↓	+
					11/15/34	L	+	−	+	+↑	−↑	+↓	+↓	−↑	+
11.	M. C.	46	♀	67280	12/10/34	L	+	−	∓	+↑	−↓	+	+↑	−↑	+
					12/12/34	L	+	−	∓	+↓	−↓	+↑	+↓	−↑	+↑
					12/13/34	L	+	−	+	+	−↑	+	+↓	−↓	+
					12/18/34	L	+	−	+	+	−↓	+	+↓	−↑	+↓

*0, no axis deviation; R, right; L, left.

† + is a positive wave, − is a negative wave, ± and ∓ are diphasic waves.

‡ ↑ means wave becomes more positive, ↓ means wave becomes less positive, when no arrow is used, the wave does not change in amplitude.

I

CHEST LEAD IN POSTURE

CHEST LEAD—B (CHEST ELECTRODE ½ WAY BETWEEN MIDSTERNAL LINE AND APEX)									CHEST LEAD—C (CHEST ELECTRODE AT APEX)									COMMENTS
SUPINE			SITTING			LYING ON LEFT SIDE			SUPINE			SITTING			LYING ON LEFT SIDE			
R	S	T	R	S	T	R	S	T	R	S	T	R	S	T	R	S	T	
+	−	+	+↓	−↑	+↑	+	−↓	+↓	+	−	+	+	−	+↓	+↓	−↓	+↓	On left side, Lead A, T becomes diphasic.
+	−	+	+	−↑	+	+↓	−↓	+↓	+	−	+	+↓	−↑	+	+↓	−↓	+↓	On left side T lowest amplitude.
+	−	+	+↑	−↑	+↑	+	−↓	+↓	+	−	+	+↑	−↑	+	+↓	−↓	+↓	On left side T lowest.
+	−	+	+↑	−↓	+↑	+↓	−↑	±↓	+	−	±	+	−↓	+	+↓	−↑	+↓	On left side, Leads A and B, T becomes diphasic.
+	−	+	+↓	−↓	+↓	+↑	−↓	+↑	+	−	+	+↓	−	+↓	+↑	−↓	+↑	Supine T highest.
									+	−	+				+↓	−↑	+↓	Supine T highest.
+	−	+	+↓	−↑	+	+↓	−↑	+	+	−	+	+↓	−↑	+↓	+↑	−	+↑	Only slight change.
+	−	+	+↓	−	+↓	+↓	−↑	+	+	−	+	+	−	+↓	+↓	−↑	+	Sitting T lowest.
+	−	+	+↓	−↓	+	+↓	−	+	+	−	+	+↓	−	+↓	+	−↓	+	Supine T highest.
+	−	+	+↓	−↑	+↓	+	−↓	+↓	+	−	+	+↓	−↓	+↓	+↑	−↓	+↓	Supine T highest.
+	−	+	+↓	−↑	+	+↓	−↓	±↓	+	−	+	+↑	−↓	+↑	+↓	−↓	±↓	On left side RS-T segment elevated and T diphasic. Digitalis—1.8 gm. on 4/14/35.
+	−	∓	+	−↑	+↑	+	−	∓↓	+	−	±	+↓	−	+↑	+↓	−↓	+↓	Supine and on left side T diphasic.
+	−	+	+↑	−↓	∓↓	+↓	−↑	+↑	+	−	+	+↓	−↓	+↓	+↑	−↑	+↑	Sitting and on left side RS-T segment elevated.
									+	−	+	+↑	−↓	+↑	+↓	−↑	+↓	Sitting T highest.
									+	−	+	+↑	−↑	+	+↓	−↓	+↓	Only slight change. Digitalis—1.6 gm. on 11/13/34.
									+	−	+	+↓	−↑	+↓	+↓	−	+↓	On left side T lowest.
									+	−	+	+↓	−↑	+↓	+	−↓	+↓	On left side T lowest.
+	−	±	+↑	−↓	+↑	+↓	−	+↓	+	−	+	+↑	−↓	+↑	+↓	−	+↓	Only slight change.
+	−	+	+↓	−↑	+↓	+↓	−↑	+↓	+	−	+	+↓	−↑	+↓	+↓	−↑	+↓	Supine and sitting RS-T segment slightly elevated.
+	−	+	+↓	−↓	+↓	+	−↓	+↓	+	−	+	+↑	−↑	+	+	−↓	+↓	RS-T segment slightly elevated throughout.
									+	−	−				+	−↑	−↑	T negative or low throughout.
+	−	+	+↓	−↑	+↓	+↓	−↑	+↓	+	−	+	+	−↑	+↓	+↓	−↑	+↓	Supine T highest.
									+	−	+	+↓	−↑	+↓	+↓	−↑	+↓	On left side T lowest.
									+	−	+	+↓	−↓	+↓	+↓	−↑	+↓	On left side T lowest. Digitalis—1.8 gm. on 11/9/34.
									+	−	+	+	−↑	+↓	+↓	−↓	+	Sitting T lowest. Digitalis—0.2 gm. per day.
									+	−	+	+↓	−↓	+↓	+↓	−↑	+↓	On left side T lowest. Digitalis—0.2 gm. per day.
+	−	+	+	−↓	+↑	+↑	−↑	+↓	+	−	+	+	−↓	+↑	+↑	−↑	+↓	On left side T lowest.
+	−	∓	+↓	−↓	+↑	+↓	−↑	+	+	−	∓	+↓	−↓	∓↓	+↓	−↑	±	T low throughout. Digitalis—1.8 gm. on 12/11/34.
+	−	+	+	−↑	··	+↑	−	+	+	−	+	+↑	−	+↑	+	−↑	+↓	T low throughout.
+	−	+	+	−↓	+	+↓	−↑	+↓	+	−	+	+	−↓	+	+↓	−↑	+J	On left side T lowest.

TABLE

CASE NO.	NAME	AGE	SEX	HOSPITAL NUMBER	DATE	AXIS DEVIATION	CHEST LEAD—A (CHEST ELECTRODE ON MIDSTERNAL LINE)								
							SUPINE			SITTING			LYING ON LEFT SIDE		
							R	S	T	R	S	T	R	S	T
12.	J. McC.	23	♂	79052	11/ 3/34	L	+	−	+	+↓	−↑	+↓	+	−	+
13.	S. L.	44	♂	74633	11/26/34	R	+	−	−	+↑	−↓	−↓	+↓	−↑	−↑
14.	C. McA.	68	♂	14258	1/15/35	0	+	−	+	+↓	−↑	+↑	+↓	−↑	+↓
					1/17/35	0	+	−	−	+↑	−↓	−	+↑	−↑	−↑
					1/19/35	0	+	−	−	+↑	−↓	−↓	+↑	−↑	∓↑
15.	W. M.	36	♂	103699	9/10/35	R	+	−	+						
					9/17/35	R	+	−	+	+↓	−↓	+	+↑	−↑	+
					9/21/35	R	+	−	+	+↓	−↓	±↓	+	−	±↓
					9/26/35	R	+	−	+	+	−	±	+↓	−↑	±
					9/30/35	R	+	−	−	+	−↓	−	+↑	−↑	−
16.	I. F.	13	♂	82012	12/11/34	L									

(Cases 6 to 8, inclusive) alterations similar to those seen in subjects whose hearts were normal occurred (Fig. 2). In most instances a decrease in the amplitude of the R and T waves took place as the subject's position was changed from supine, to sitting, to lying on the left side. In several instances an upright T wave became diphasic. In Case 6 the RS-T segment twice became elevated (second and fourth records, April 15, 1935 and April 19, 1935) when the subject lay on the left side.

(4) Changes in patients with rheumatic lesions of both the mitral and the aortic valves and predominant enlargement of the left ventricle.—In these cases (Cases 9 to 12, inclusive) the variations in amplitude of the R and T waves were similar to those seen in subjects with normal hearts, but more marked (Fig. 3). The S wave, however, in these cases of left ventricular preponderance, showed a definite tendency to decrease in amplitude with change in position from supine, to sitting, to lying on the left side. In Case 11 the second record (December 12, 1934) showed diphasic T waves in leads A and B with the patient in the supine position which became upright when he sat up or lay on the left side.

(5) Changes in a patient exhibiting emphysema and enlargement of the right ventricle.—In this patient (Case 13) the T waves were negative; the changes in the amplitude of the R and T waves were similar, however, to those which occurred in patients with rheumatic heart disease and right ventricular preponderance.

I—CONT'D

CHEST LEAD—B (CHEST ELECTRODE ½ WAY BETWEEN MIDSTERNAL LINE AND APEX)						CHEST LEAD—C (CHEST ELECTRODE AT APEX)						COMMENTS
SUPINE			SITTING			LYING ON LEFT SIDE			SUPINE			SITTING			LYING ON LEFT SIDE			
R	S	T	R	S	T	R	S	T	R	S	T	R	S	T	R	S	T	
									+	−	+				+↓	−↑	+↓	Supine T highest.
+	−	−	+↑	−	−↓	+↓	−	−↑	+	−	−	+↑	−↓	−↓	+↓	−↑	−↑	Sitting T lowest.
+	−	+	+↓	−	+	+	−↑	+	+	−	+	+↓	−	+	+	−↑	+↓	Only slight change.
+	−	−	+↑	−↑	−↓	+↑	−↑	∓↑	+	−	−	+↑	−↓	−↓	+↑	−↑	∓↑	On left side T negative or diphasic. Digitalis—1.7 gm. on 1/16/35.
+	−	−	+	−↓	−↓	+↑	−↑	∓↑	+	−	−	+	−↓	−↓	+↑	−↓	∓↑	On left side T negative or diphasic.
+	−	±							+	−	−							Only slight change.
+	−	±	+	−	±↓	+↑	−↑	±	+	−	±	+↓	−↑	±	+↑	−	±↑	In Leads B and C, T diphasic.
+	−	±	+↑	−↓	±↓	+	−↑	−	+	−	±	+	−	±↓	+↓	−↓	−	On left side: Lead A, T becomes diphasic; Leads B and C, T becomes negative.
+	−	±	+	−↑	−↓	+↑	−	−↓	+	−	±	+↑	−	−↓	+↓	−↓	−	On left side: Lead A, T becomes diphasic; Leads B and C, T becomes negative.
+	−	−	+↓	−	−↑	+↑	−	−	+	−	−	+↓	−↓	−↓	+↑	−↓	−	Only slight change. Digitalis—1.8 gm. on 9/28/35.
									+	−	±	+↓	−↑	±	+↑	−↓	±↓	On left side RS-T segment becomes slightly elevated.

(6) Changes in a patient suffering from arteriosclerotic heart disease without cardiac enlargement.—In Case 14 the T waves were negative or diphasic in the second and third records (January 17, 1935 and January 19, 1935). They were inclined to be most negative with the patient in the sitting position, and, in leads B and C, became diphasic instead of negative when the subject lay on the left side.

(7) Changes in patients suffering from chronic constrictive pericarditis.—These patients (Cases 15 and 16) showed only slight variations in the amplitude of the R, S, and T waves with change in posture. This may be attributed to the relative fixation of the heart which was shown to occur in such cases by Stewart and his associates,[12, 13] as well as by Cushing and Feil.[14] In Case 15, however, the T waves changed from positive to diphasic in lead A, and from diphasic to negative in leads B and C.

(8) Observations relating to digitalis.—In six patients (Cases 6, 7, 10, 11, 14, and 15), chest leads were taken both before and after therapeutic doses of digitalis had been given. Those taken after the administration of the drug showed the changes described by Stewart and Watson,[15] but the variation in the amplitude of the R, S, and T waves in response to change in posture showed no deviation from the trend seen in the chest leads taken before the drug was given.

COMMENTS

Our observations show that the form of the chest lead varies with change in posture both in normal subjects and patients with heart disease, regardless of the size of the heart or the deviation of the electrical axis. The changes were less marked in cases of chronic constrictive pericarditis, in which the position of the heart was relatively fixed. The general trend was toward progressive decrease in the amplitude of the R and T waves as the subject's position was changed from supine, to sitting, to lying on the left side. The T waves, in some cases, became diphasic instead of positive, and negative instead of diphasic (Fig. 4).

Although the variation in amplitude of the waves of the chest leads followed certain trends, as has been pointed out, neither the amplitude nor the direction of the change could be predicted with any certainty in individual cases. Moreover, patients often showed different variations on subsequent days.

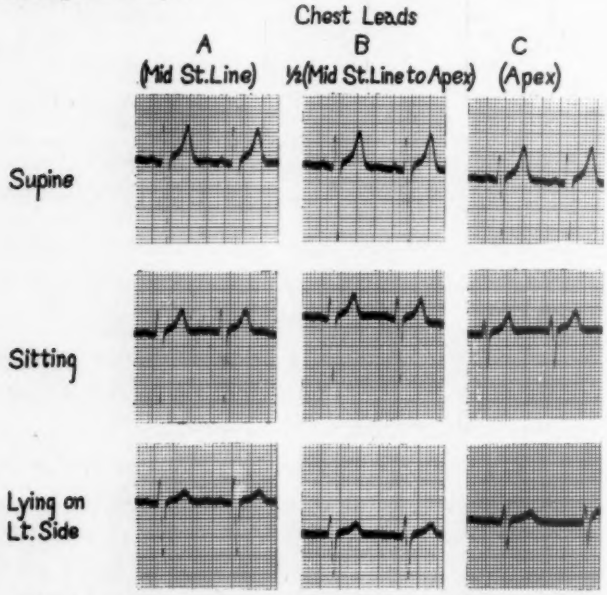

Fig. 3.—In this figure the chest leads of H. W. (Case 9), taken Jan. 4, 1935, are reproduced. The records in this case serve to illustrate the change that occurred in the chest leads of patients exhibiting left ventricular preponderance. There was a decrease in the amplitude of the R waves and T waves, and a decrease in the amplitude of the S waves, as the patient's position was changed from supine, to sitting, to lying on the left side. The change in these cases was more marked than in patients with normal hearts.

Fig. 5 shows the magnitude, frequency, and direction of change in amplitude of the waves of chest leads taken in different positions. A comparison of chest leads taken with the patient in the supine and sitting positions (upper three figures) showed that there was a tendency for the R and T waves to be lower in the leads taken in the sitting position. The S wave, however, followed no trend. A comparison of chest leads taken with the patient in the supine position and lying on the left side (middle three figures) showed a more marked

tendency for the R and T waves to be of lower amplitude in the leads taken with the patient lying on the left side. The S wave also showed a tendency to decrease in amplitude when the patient's position was changed from supine to lying on the left side. A comparison of chest leads taken with the patient in the sitting position and lying on the left side (lower three figures) showed again the tendency of the R, S, and T waves to decrease in amplitude as the patient's position was changed from sitting to lying on the left side. All of these changes were slightly more marked in Chest Lead C than they were in Chest Leads A and B.

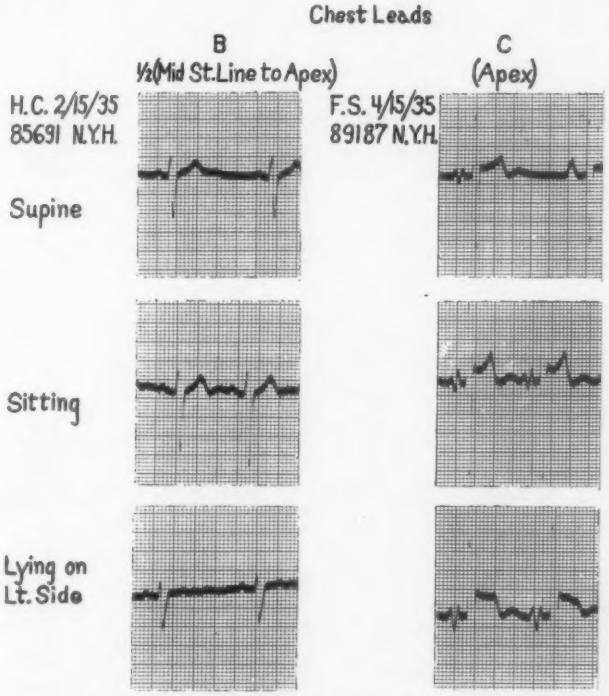

Fig. 4.—In Fig. 4*B*, Chest Lead B, of H. C. (Case 2), taken Feb. 15, 1935, and in Fig. 4*C*, Chest Lead C, of F. S. (Case 6), taken April 15, 1935, are reproduced. The records in these cases serve to illustrate the change in the form of the T waves and RS-T segments that occurred in some instances (Cases 1, 2, 6, 14, 15, and 16). The T wave may become diphasic instead of positive, or the RS-T segment may become elevated, as the patient's position is changed from supine, to sitting, to lying on the left side.

In certain instances sufficient change occurred in the form of the chest lead with change in the posture of the subject to confuse or alter the interpretation of the electrocardiogram. This was observed most frequently when the exploring electrode was placed at the apex (Chest Lead C). In the interpretation of precordial leads, the posture of the patient must be taken into account.

SUMMARY

1. Chest leads were taken with subjects in three positions: supine, sitting, and lying on the left side,

2. Three precordial leads were used. In one, the exploring electrode was placed in the midsternal line at the level of the fourth intercostal space (Chest Lead A); in the second, halfway between this point and the apex (Chest Lead B); and in the third, at the apex (Chest Lead C). In each case, the indifferent electrode was in the interscapular region.

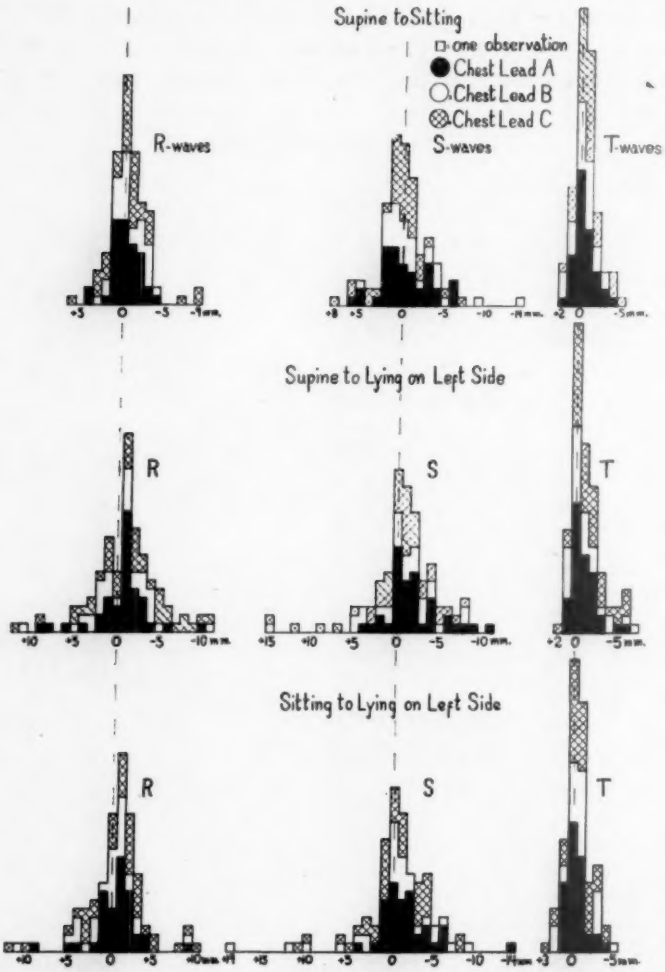

Fig. 5.—Variations in the amplitude of the R, S, and T waves of Chest Leads A, B, and C are presented in this figure as frequency diagrams. Each of the three positions (supine, sitting, and lying on the left side) is compared with each of the other two positions. The upper three figures show the variations in amplitude of the R, S, and T waves of the chest lead when the patient's position was changed from supine to sitting; the middle three figures illustrate the variations that occurred when the position was changed from supine to lying on the left side; and the lower three figures show the changes which occurred when the position was changed from sitting to lying on the left side. The solid portions of each figure are the changes that occurred in Chest Lead A, the clear portions are the changes that occurred in Chest Lead B, and the shaded portions those that occurred in Chest Lead C. Each square represents a comparison of the same wave of corresponding chest leads taken with the patient in different positions. The change in amplitude in millimeters is plotted along the abscissae, the frequency of the change, along the ordinates.

3. Forty-one observations were made on sixteen patients. The group included normal subjects and patients with heart disease. Among the latter were patients with right, and others with left, ventricular preponderance. In three patients the position of the heart was relatively fixed.

4. The variations in the form of the chest lead with change in the patient's posture are described. They consisted chiefly of a decrease in the amplitude of the R and T waves, which varied concordantly, and, in many cases, a decrease in the amplitude of the S waves, as the subject's posture was changed from supine, to sitting, to lying on the left side. In several cases positive T waves became diphasic and diphasic T waves became negative.

5. Although these changes occurred in each of the three chest leads, they were most marked in Chest Lead C (electrode at apex).

6. The changes cannot be predicted with any certainty in individual cases.

7. The importance of considering the patient's position when taking chest leads, and of taking them in the same position each time in order to make them comparable, is pointed out.

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INFRARED PHOTOGRAPHIC DEMONSTRATION OF THE SUPERFICIAL VENOUS PATTERN IN CONGENITAL HEART DISEASE WITH CYANOSIS*

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INFRARED photographic demonstration of the superficial veins already has acquired definite diagnostic value. The numerous prominent veins visualized in infrared photographs of patients with increased intra-abdominal pressure due to large tumors, ascites, or advanced pregnancy present an appearance different from the normal superficial venous pattern, which is usually composed of a few narrow, scattered veins. In cirrhosis of the liver the superficial venous pattern becomes more complex and prominent because of portal hypertension. This occurs in the absence of ascites, also, and is considered a satisfactory confirmatory sign.[1]

PROCEDURE

All three patients reported here have congenital heart disease with cyanosis, clinically diagnosed as Fallot's tetralogy. Infrared photographic studies were made to determine whether any abnormalities of the superficial venous system could be demonstrated in this type of heart disease. Control photographs of each patient were made with panchromatic film. In addition, studies of normal individuals and of patients with compensated and decompensated rheumatic and nonrheumatic heart disease were made. One patient with cor pulmonale secondary to bronchiectasis was studied in a similar manner.

The infrared photographs were taken with a film-pack camera, using 6.5 x 9 cm., Eastman, infrared-sensitized plates. The lens was stopped down to f:11 after the image had been focused on the ground-glass screen. A red filter was then placed in front of the lens. Illumination was secured from four "photoflood" bulbs (500 watts each), set in aluminum reflectors and placed about 5 feet from the patient at 45-degree angles. An exposure of from 1/10 to ½ second was found adequate, depending on the lens aperture. The plates were developed in x-ray processing solutions in total darkness, according to the manufacturer's directions. Projection prints were made on No. 4 glossy paper.

CASE REPORTS

CASE 1.—J. B., a 7-year-old boy, complained of dyspnea on slight exertion. He had been a normal infant, and was apparently in good health until the age of 3 months. At that time cyanosis of the lips became evident, and progressed until he had a generalized dusky hue, most marked over his face. His growth had been normal. Within the preceding year there had been a rapid, progressive decrease of exercise tolerance. He was in a fair state of nutrition and of average mentality.

His heart rhythm was normal. A loud, blowing systolic murmur was heard over his entire precordium. His neck veins were not distended. Advanced clubbing of the fingers and toes, with cyanosis of the nail beds, was present.

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Roentgenologic examination of his chest revealed a sabot-shaped heart. This was most apparent when observed fluoroscopically with the patient rotated slightly into the right anterior oblique position. The hilar vascular shadows were diminished.

An electrocardiogram showed marked right axis deviation, with slurring of the main ventricular complexes in Lead II. The auriculoventricular conduction time was 0.22 second.

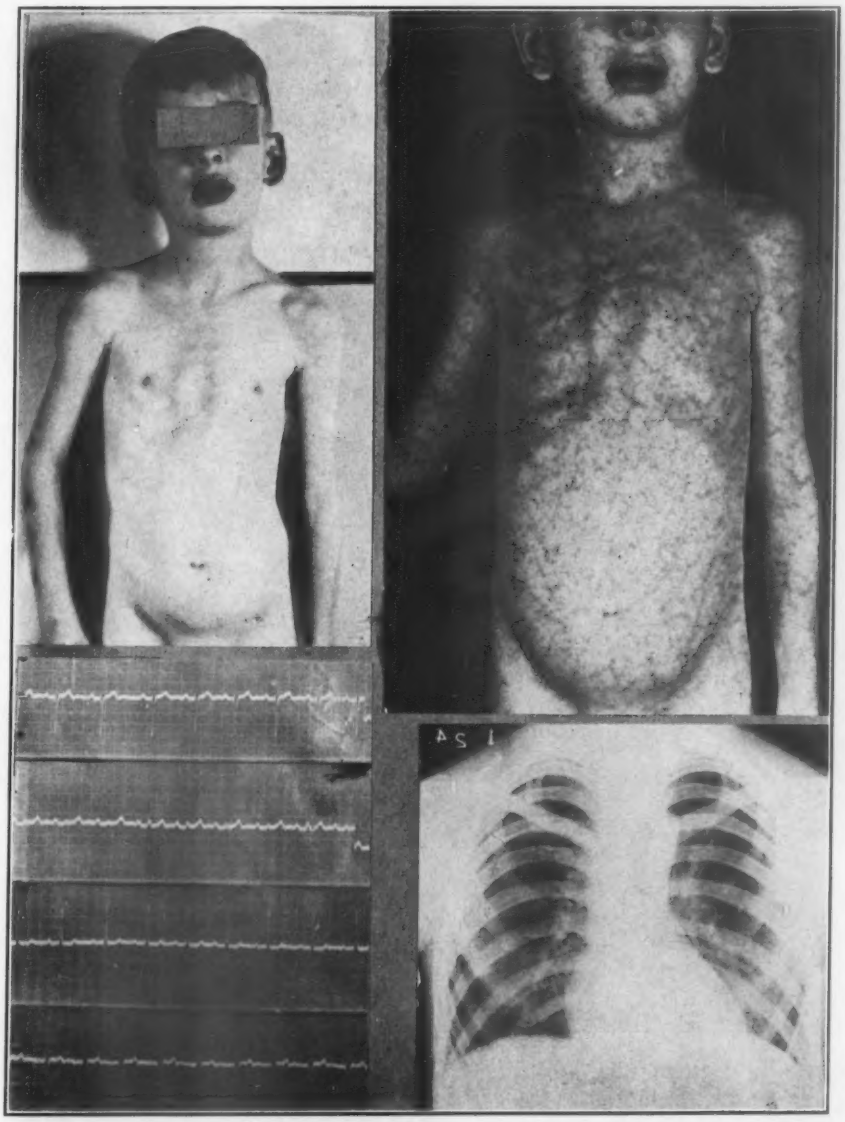


Fig. 1.—*A*, routine photograph on panchromatic film. *B*, infrared photograph, showing prominence and complexity of the superficial veins. *C*, electrocardiogram, showing right axis deviation. *D*, teleoroentgenogram.

A photograph on panchromatic film showed a trace of a vein over his chest, which was seen better on direct inspection. An infrared photograph revealed re-

markable prominence and tortuosity of the entire superficial venous network. Direct inspection of the patient gave no hint as to the extent or enormous complexity of his superficial veins.

CASE 2.—H. S., a 22-year-old girl who was known to have had heart disease since birth, was hospitalized because of weakness and dyspnea. Until the age of 16 she had been able to indulge in moderately strenuous exercise. At that time she developed migratory arthritis, and her activities were curtailed. Dyspnea on exertion appeared soon thereafter, and she had been confined to a bed or chair ever since. Several attacks of congestive heart failure, with enlargement and tenderness of the liver, were relieved by diuretics and digitalis. On several occasions she had had hemoptysis with chest pain, suggesting pulmonary embolism.

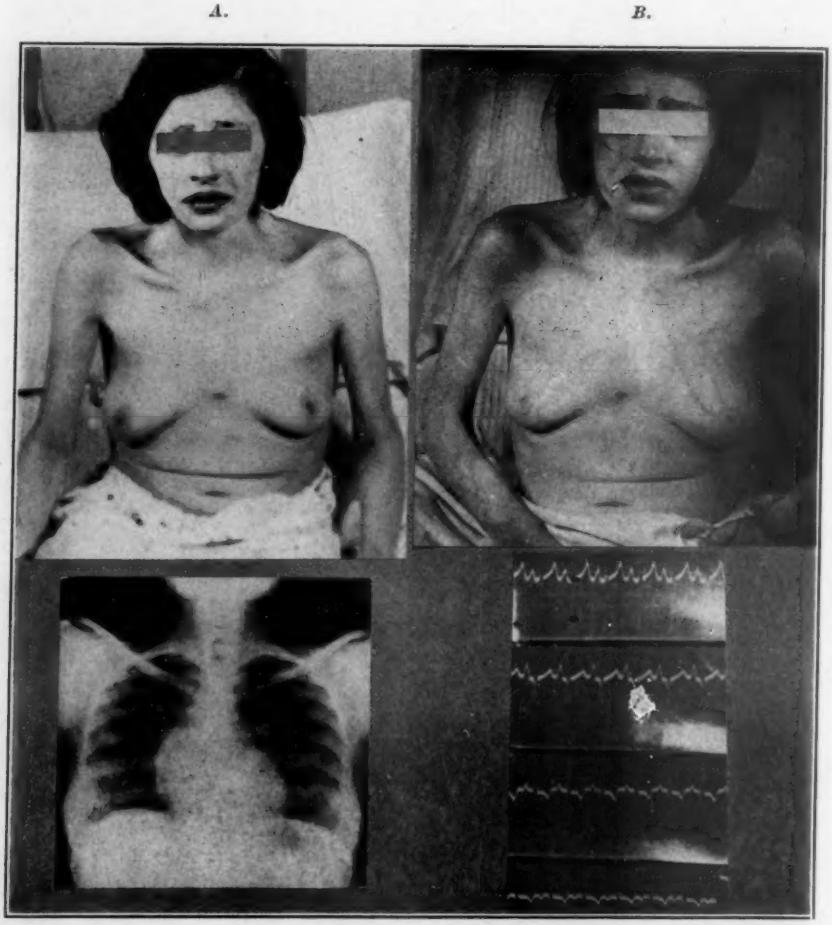


Fig. 2.—*A*, routine photograph on panchromatic film. *B*, infrared photograph, showing prominent superficial veins. *C*, teleoroentgenogram. *D*, electrocardiogram, showing right axis deviation.

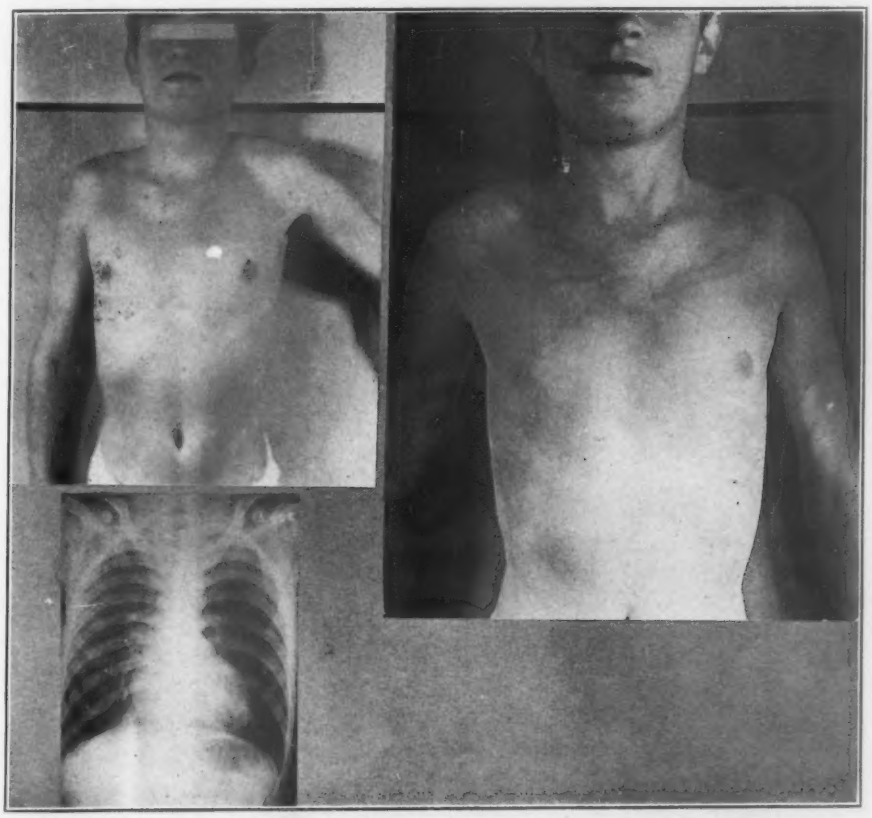
She was rather small and poorly nourished, but normally developed. Her mental abilities and interests were average. Intense cyanosis of the lips and circumoral tissues was present. The remainder of the body had a dusky tinge. Marked clubbing of the fingers and toes was present. Her heart rhythm was normal. A loud, blowing systolic murmur, most intense over the pulmonic area and to the

left of the sternum, was present. Her neck veins were not distended. Her blood pressure was 110/70. She had polycythemia, with 7.5 million erythrocytes and a hemoglobin of 120 per cent.

Roentgenologic examination of her chest revealed a sabot-shaped heart, the contour of which was best seen with the patient rotated slightly into the right anterior oblique position. Her electrocardiogram showed marked right axis deviation, with high P waves in Leads I and II. The main ventricular complex in Lead II was inverted. The T waves in Lead I were high and were inverted in Lead III.

She was believed to have rheumatic heart disease superimposed on the congenital cardiac malformation.

A. *B.*



C.

Fig. 3.—*A*, routine photograph on panchromatic film. *B*, infrared photograph, showing prominent superficial veins. *C*, teleoroentgenogram.

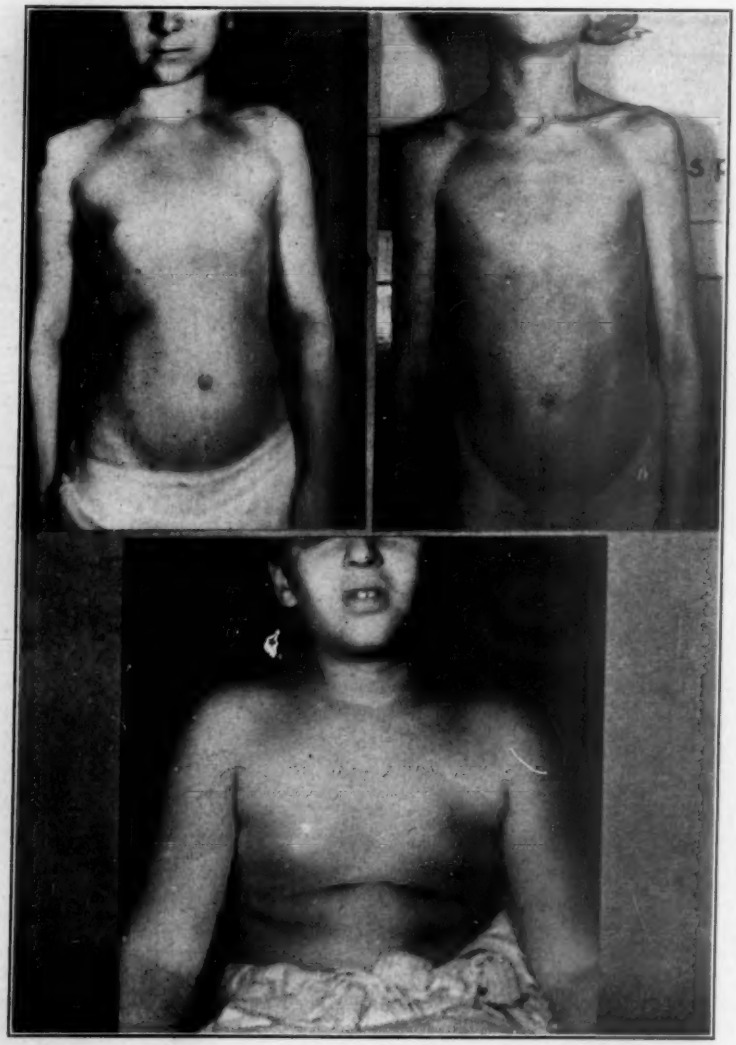
A routine photograph did not show the few veins visible over the breasts. An infrared photograph, however, showed a marked increase in the number and size of the veins over the entire area photographed. This was not as pronounced as in the first patient, possibly because of the difference in the thickness of the superficial tissues of a 22-year-old woman and a 7-year-old boy.

CASE 3.—H. Z., 19 years of age, had been dyspneic on slight exertion since the age of 12. Cyanosis of the lips and fingers was first seen when he was 6 months old. Clubbing of the fingers and toes appeared at the age of 3 years. The patient

could not walk until he was 6 years old because of weakness. After that time he could indulge in moderate exercise. Since the age of 11, following a fall caused by dizziness, he had been confined to bed or a chair. Edema of the ankles was noted when he was 12 years old.

The patient was frail and appeared young for his age. His mentality was considered above average. Cyanosis of the oral and circumoral tissues was marked, and the remainder of his body had a dusky appearance. A systolic murmur was audible over the entire precordium, loudest at the pulmonic area. His neck veins

A. *B.*

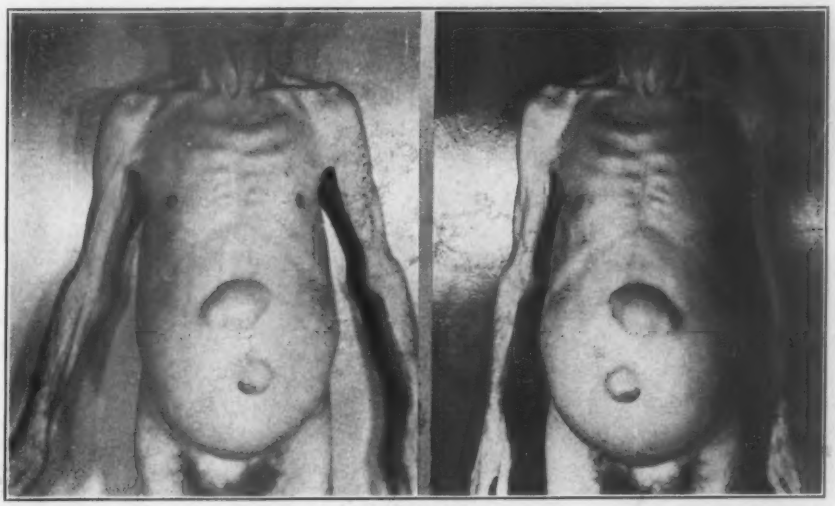


C.

Fig. 4.—*A*, girl, 12 years old, with no evidence of organic heart disease. Infrared photograph shows no dilated superficial veins. *B*, boy, 10 years old, with rheumatic fever and mitral insufficiency. There were no evidences of congestive failure. Infrared photographs show no dilated superficial veins. *C*, boy, 11 years old, with active rheumatic fever and no evidences of cardiac involvement. Infrared photograph shows no dilated superficial veins.

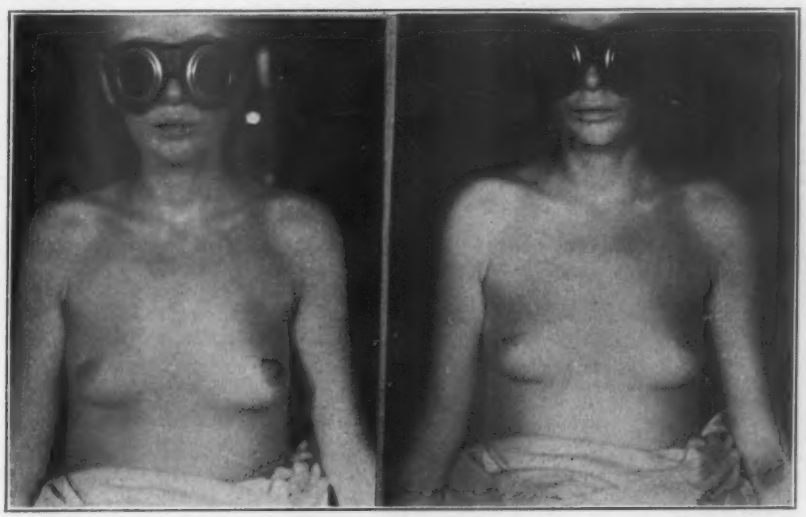
were not unduly prominent. The blood pressure was 106/70. His liver and spleen were not palpable. Inspection of his eye grounds showed marked distention of the retinal veins. A polycythemia of 8.2 million erythrocytes, with a hemoglobin of 125 per cent, was present.

Radiographic examination of the chest and electrocardiographic study revealed abnormalities very similar to those in Cases 1 and 2.



A. *B.*

Fig. 5.—*A*, man, 65 years old, with hypertensive and arteriosclerotic heart disease. No clinical evidences of heart failure were present when this film was taken. Photograph on panchromatic film. *B*, infrared photograph shows no evidences of dilated superficial veins.



A. *B.*

Fig. 6.—*A*, 16-year-old girl with rheumatic fever, mitral stenosis and insufficiency, and aortic insufficiency. Had had several attacks of congestive failure, and was in failure when this photograph was taken. *B*, infrared photograph shows slightly dilated veins over the chest and shoulders. Note the left elbow region, with an ecchymotic area due to vein puncture.

A routine photograph of the chest did not show the single, visible, dilated vein which was present. An infrared photograph, however, revealed a marked increase in the number and size of the veins over the area photographed.

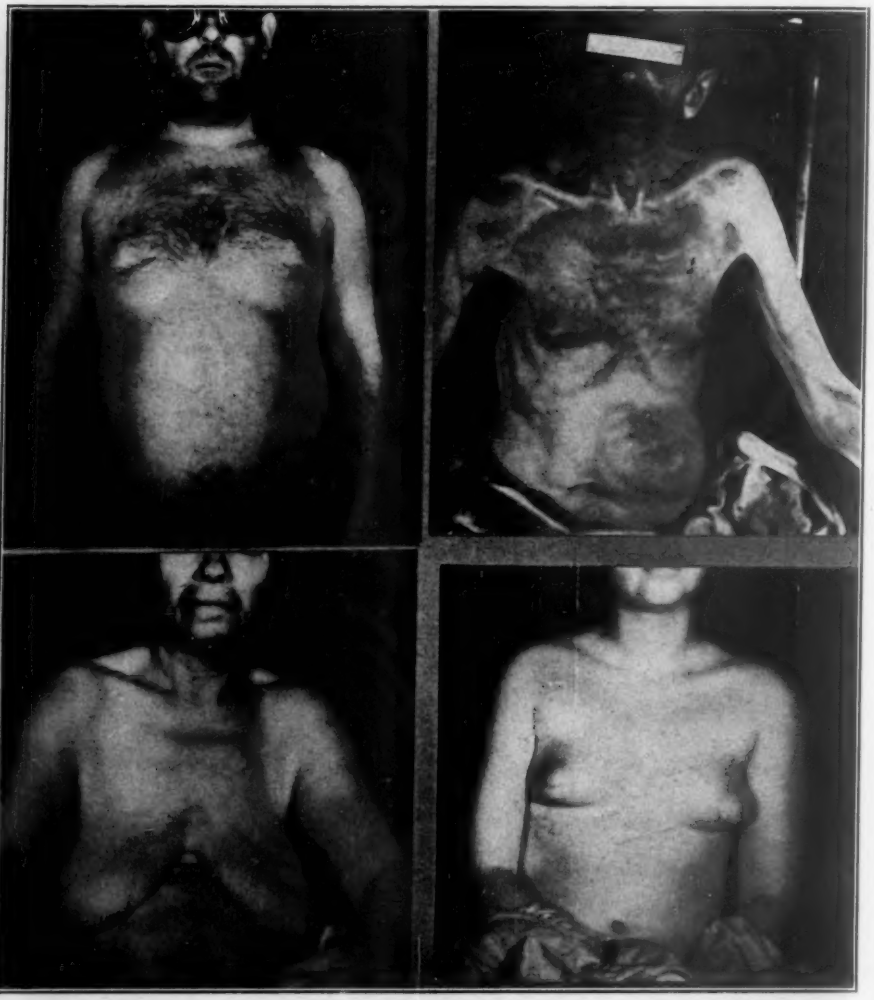


Fig. 7.—*A*, 40-year-old man with mitral stenosis and insufficiency and aortic insufficiency. He was ambulatory, classified as II B. Infrared photograph shows a few dilated veins over the arms. *B*, 64-year-old man with bronchiectasis for many years; clinical diagnosis was cor pulmonale, with right-sided heart failure. His liver was enlarged, ankle edema was present, and he was cyanotic. Electrocardiogram showed auricular fibrillation and right axis deviation. Infrared photograph shows some dilated veins over both shoulders and the left arm, but the dilatation is not marked. *C*, 66-year-old woman just recovering from a coronary seizure. Photograph taken day after patient had been removed from an oxygen tent. Patient still cyanotic. Electrocardiogram showed left bundle branch block. Infrared photograph, showing veins over the breasts which can also be seen on inspection. No dilated superficial veins are seen over the thorax. *D*, a 16-year-old girl with active rheumatic fever, mitral stenosis and insufficiency, and aortic insufficiency, in congestive failure. A minimal number of small veins visible over the upper thorax and shoulders. Infrared photograph.

COMMENT

Each of the three patients mentioned above had congenital heart disease of the Fallot's tetralogy variety. No evidences of congestive heart failure or increased venous pressure were present when the photographs were taken. Examination of the eye grounds of one patient showed marked distention of the retinal veins.

Infrared photographs visualized prominent and tortuous superficial veins in each patient. The extent of this abnormality had not been anticipated nor suspected before the infrared photographs were made.

Control studies on several normal subjects, and patients with rheumatic and hypertensive heart disease, both with and without congestive failure, did not show similar superficial venous abnormalities. It is interesting to note that the patients with decompensated organic heart disease and the patient with cor pulmonale showed an increase of moderate degree in the number and size of the veins over the shoulders and arms. This may be a reflection of the increased pressure in the right auricle.

White[2] states that cyanosis in "maladie bleu" is dependent on three factors: (a) the shunt of the venous blood into the systemic circulation, (b) dilatation of the skin and superficial mucous membrane capillaries, with peripheral slowing of the blood stream, and (c) insufficient oxygenation of the blood in the lungs.

The present study indicates the possibility of a fourth cause, which may be only an extension of the second reason for cyanosis advanced by White. This, as suggested by the infrared photographs, is a congenital abnormality of the superficial venous tree which may be related to the cardiac malformation.

Prominence of the superficial veins in patients with abdominal tumors is believed to be due to increased intra-abdominal pressure, and similar patterns in patients with cirrhosis of the liver are believed to be secondary to portal hypertension, with development of a collateral circulation. It is important to note that no clinical evidences of increased venous pressure were present in the patients reported here, and despite this fact the number and size of the veins were greatly increased.

SUMMARY

A marked increase in the number and size of the superficial veins was demonstrated by means of infrared photography in three patients who had congenital heart disease with cyanosis.

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PLETHYSMOGRAPHIC STUDIES OF PERIPHERAL BLOOD FLOW IN MAN

III. Effect of Smoking Upon the Vascular Beds in the Hand, Forearm and Foot*

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THE role of tobacco smoking in the production of organic changes in the cardiovascular system has been the subject of extensive laboratory and clinical research, but, as pointed out by Thienes and Butt,[1] most of the early work cannot be properly evaluated because of the lack of adequate controls. Nevertheless, it has been fairly well established that smoking does cause peripheral vasoconstriction, as indicated both by lowering of skin temperature[2-5] and by plethysmographic measurements showing diminished blood flow.[6, 7] Unfortunately, since the temperature of the skin depends for the most part upon the rate of blood flow through the superficial vessels, and since the above-mentioned plethysmographic studies were performed upon the hand, in which there are many cutaneous blood vessels capable of responding to stimuli, very little information can be derived from such work as to the effect of smoking upon the arteries and arterioles in the muscles. In view of the involvement of the latter vessels in thromboangiitis obliterans and other vascular disorders of the extremities, it was thought worthwhile to re-investigate this subject by making plethysmographic studies of the forearm, which consists principally of muscle.

METHOD

Nine normal subjects and thirteen patients‡ with various types and degrees of peripheral vascular disease were studied. Most of the subjects were tested repeatedly. With the exception of three nonsmokers (F. M., J. M., and M. M.), all were habitual smokers who had abstained for at least two hours before the test. Plethysmographic studies were generally made on two extremities simultaneously; the method employed was essentially the same as that described in previous reports.[8, 9] In the case of the upper extremity, only the upper portion of the forearm was enclosed in the plethysmograph; the wrist and hand were immersed in water in an outer chamber. The temperature of the room was maintained between 25 and 27° C. (unless otherwise indicated), and the temperature of the water in the plethysmographs (to be designated hereafter as bath temperature)

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‡A number of the patients were obtained from the Peripheral Vascular Clinic of the Mount Sinai Hospital.

was either 32° or 45° C. If reflex vasodilatation in one of the extremities in the plethysmographs was desired, the bath temperature in the other plethysmograph was raised to 45° C, a third extremity was generally immersed in water at the same temperature, and the subject was covered with blankets. Blood flow measurements were made only after reflex vasodilatation, as indicated by generalized sweating, had been present for at least fifteen minutes.

Ten to fourteen control blood flow measurements were obtained by applying a venous occlusion pressure to the limb, proximal to its insertion into the plethysmograph, and recording upon a kymograph the rate of increase in extremity volume. The subject was then permitted to smoke one or two cigarettes of a common brand; during this time (generally about six to eight minutes) and for the following half hour, blood flow measurements were made at short intervals. In the case of the forearm, a blood pressure cuff was also applied to the wrist, as advocated by Grant and Pearson,[10] and a pressure of 200 mm. Hg was applied just before, and maintained during, the blood flow determination; in a number of instances, however, this cuff was left deflated for some of the records. The reason for these steps will be discussed below. During the period of smoking blood flow determinations were generally obtained at least one minute after cigarette puffs, in order to minimize the vasoconstrictor effect of the associated deep breath.

RESULTS

1. *Effect of Smoking Upon Blood Flow in the Hand.*—At a bath temperature of 32° C. (Table I, Fig. 1), all thirteen trials in normal subjects showed definite or slight reductions in blood flow either during or immediately following the period of smoking. Among the patients suffering from peripheral vascular disease (as detailed in the tables), six trials demonstrated a significant, and five a slight, decrease. In three of the latter the flow was small before smoking. In three others no response was elicited, and, similarly, in two of these the initial flow was small. In the remaining two patients in the abnormal group (F. M. and O. C.), both of whom had hypertension, there was an increase in blood flow. In the reflexly vasodilated hand (Table II, Fig. 2), smoking produced a decrease in five trials on normal subjects and no effect in another. In the abnormal group there were a decrease in two and a slight increase in one; in the latter the flow before smoking was small. At a bath temperature of 45° C. (Table III, Fig. 3), in the normal group there were a decrease in three, no effect in two, and an increase in another. In the abnormal group there were a decrease in two trials and no significant effect in one.

2. *Effect of Smoking Upon Blood Flow in the Forearm and Hand Together.*—In this group, the blood pressure cuff at the wrist was not inflated before making the blood flow measurement. Under these circumstances, as pointed out by Grant and Pearson,[10] the swelling of the forearm produced by the application of the venous occlusion pressure is influenced not only by the rate of arterial flow into the part of the extremity enclosed in the plethysmograph, but also by venous return from the hand; obviously, then, changes in the caliber of the vessels in the hand will indirectly affect the rate of increase of the forearm volume.

TABLE I

EFFECT OF SMOKING UPON BLOOD FLOW AT A BATH TEMPERATURE OF 32° C.

SUBJECT	HAND			FOREARM-HAND			FOREARM			FOOT-LEG			REMARKS
	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	
V. B.				7.2	5.2	7.3				4.0	2.8	2.4	Normal
L. S.	16.2	16.1	15.2							3.0	1.2	2.2	Normal
	22.6	13.2	13.0							3.6	3.3	3.1	
	24.0	18.1	29.3							4.3	2.7	3.7	
				7.8	5.4	3.5				5.5	5.3	5.0	
	2.7	2.6	1.6	2.3	2.3	1.4	0.9	0.95	1.3				Room temp. 21.5° C.
	14.4	8.2	10.4	8.5	5.3	6.0	2.6	2.9	2.6				
	13.8	12.4	12.2	6.5	6.8	6.4	3.1	3.0	3.1				
	14.8	9.7	13.1	3.5		3.3							
A. R.				5.8	8.9	6.5				3.1	2.1	2.0	Normal
	15.1	13.5	13.0							2.0	2.1	2.3	
H. C.	13.0	5.8	9.5	10.0	5.4	6.4	3.9	4.1	3.9				Normal
	15.9	9.8	13.3	6.1	3.7	4.4	1.1	1.1	1.3				
C. R.	7.3	6.5	7.0	4.6	4.2	3.6	1.8	2.0	1.7				Normal
M. M.	12.3	6.9	13.2	3.6	3.5	4.7	1.3	1.6	1.8				Normal, nonsmoker, didn't inhale
L. C.	12.0	7.8	10.7	5.5	3.8	5.8	1.3	1.3	1.2				Normal

TABLE I—CONT'D

L. M.	12.1	6.1	6.5							4.5	4.2	3.6	Generalized arteriosclerosis
	3.2	3.2	2.9							2.5	2.3	2.0	
				9.1	6.4	5.2				4.2	4.2	3.7	
	9.2	5.9	6.0							3.2	2.5	2.5	
	6.9	5.3	4.2							4.0	3.4	3.2	
	3.9	2.0	3.5	4.2	3.7	4.7	1.5	1.8	1.8				Sympathectomized hand
L. F.	2.9	2.0								2.2	1.9		Generalized arteriosclerosis
	3.1	2.3	2.0							2.6	2.6	2.5	
G. M.				5.3	4.4	5.4				2.3	2.3	2.5	Hypertension
F. M.	13.2	15.0	15.0							1.4	2.1	1.7	Hypertension, nonsmoker, didn't inhale
M. B.	12.7	7.8								1.9	2.1		Terminal artery disease
A. K.	32.2	20.5								5.2	3.5		Thromboangiitis obliterans of lower extremity
S. S.	4.7		4.2										Thromboangiitis obliterans of lower extremity
J. D.	13.9		6.9							7.6		8.4	Scleroderma of upper extremity
O. C.				3.8	4.8	4.8	2.6	2.6	2.0	1.4	1.4	1.7	Hypertension
	4.5	6.1	5.4	2.9	4.1	4.8	1.5	2.3	1.5				
F. T.	16.0	15.1		12.6	9.9	11.3	4.7	4.8	5.2				Postural hypotension
J. M.	9.1	5.2	9.4										Syringomyelia, normal extrem.
	15.2	14.2	15.2										Abnormal extrem.—loss of pain and temp. sense—warmer than other

All figures represent blood flow per min. per 100 c.c. limb volume. Room temp. between 25° to 27° C. except when otherwise indicated.

TABLE II

EFFECT OF SMOKING UPON BLOOD FLOW IN A REFLEXLY DILATED EXTREMITY AT A BATH TEMPERATURE OF 32° C.

SUBJECT	HAND			FOREARM-HAND			FOREARM			FOOT-LEG			REMARKS
	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	
L. S.	26.8 29.3 25.3	22.6 25.6 17.1	24.8 31.4 24.6	10.9 12.6	11.1 10.8	9.3 11.9	2.4	2.9	2.7	9.1	9.4	8.7	Normal
A. R.	18.7	18.4	19.5	11.1	17.1	14.5							Normal
M. M.	27.9	22.8	23.5	5.6	4.8	5.5	0.8	1.0	1.1				Normal, nonsmoker, didn't inhale
H. C.	15.9	12.9	15.0	12.0	8.1	9.7	7.6	7.2	7.3				Normal
C. R.				5.4	6.2	6.5	1.2	1.4	1.3				Normal
L. M.	4.5 11.0	5.7 9.4	4.6 11.4	10.4	8.4	8.6							Generalized arteriosclerosis
L. F.	10.5	5.0	6.1							4.1	4.3	4.3	Generalized arteriosclerosis
K. M.				8.4	6.5	5.4							Hypertension
C. S.										4.6		3.5	Thromboangiitis obliterans of lower extremities

All figures represent blood flow per min. per 100 c.c. of limb volume. Room temp. 25° to 27° C.

As a result, blood flow measurements thus obtained reflect, to some extent, a combined response of the blood vessels in the hand and forearm. At a bath temperature of 32° C. (Table I, Fig. 1), in the normal group there were a decrease in eight instances, an increase in one, and no effect in three. In two of the latter there was initially a small blood flow. In the abnormal group, there were a definite decrease in flow in two instances, a slight decrease in two, and an increase in two others. The two trials in which an increase in flow was obtained were performed upon a patient with hypertension. In the reflexly vasodilated extremity (Table II, Fig. 2), with normal subjects there were a decrease in flow

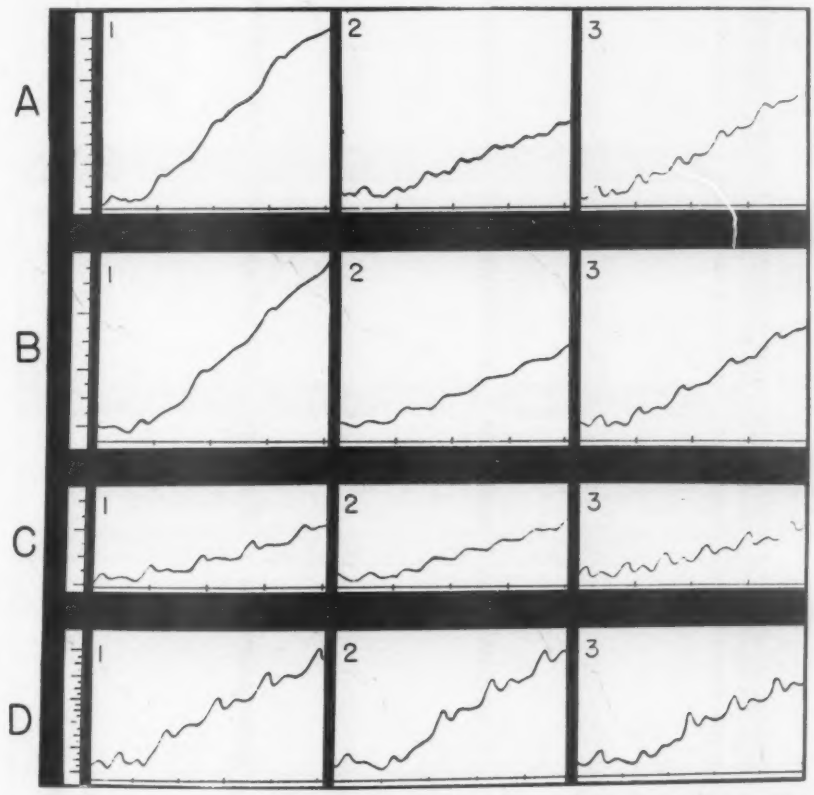

Fig. 1.—Effect of smoking upon blood flow in various blood vessel beds at a bath temperature of 32° C. *A*, Blood flow in hand (vol. 566 c.c.): *1*, before, 13.0 c.c.; *2*, during, 5.8 c.c.; *3*, after, 9.5 c.c. *B*, Blood flow in forearm (vol. 550 c.c.) together with hand: *1*, before, 10.1 c.c.; *2*, during, 5.4 c.c.; *3*, after, 6.4 c.c. *C*, Blood flow in forearm alone; *1*, before, 3.9 c.c.; *2*, during, 4.1 c.c.; *3*, after, 3.9 c.c. *A*, *B*, and *C* were obtained in a normal subject (H.C.) at one sitting. *D*, Blood flow in foot and adjoining portion of leg (vol. 1250 c.c.): *1*, before, 5.5 c.c.; *2*, during, 5.3 c.c.; *3*, after, 5.0 c.c. *D* obtained in a normal subject (L.S.). All figures represent blood flow per min. per 100 c.c. of limb vol. Time in seconds. Calibrations in 0.25 c.c.

in three instances, no effect in one, and an increase in two others. In the abnormal group there was a decrease in both cases. At a bath temperature of 45° C. (Table III, Fig. 3), in the normal group there were a slight increase in two cases and a slight decrease in two others.

3. *Effect of Smoking Upon Blood Flow in the Forearm Alone.*—In this group, by means of the blood pressure cuff, a pressure of 200 mm. Hg was applied to the wrist before, and maintained during, the actual period of blood flow measurement. This permitted alterations in blood flow to be attributed to vasomotor changes in the forearm alone, for it is apparent that venous drainage from the hand could not take place under these circumstances. At a bath temperature of 32° C. (Table I, Fig. 1), in every instance (twelve trials) there was either no effect upon

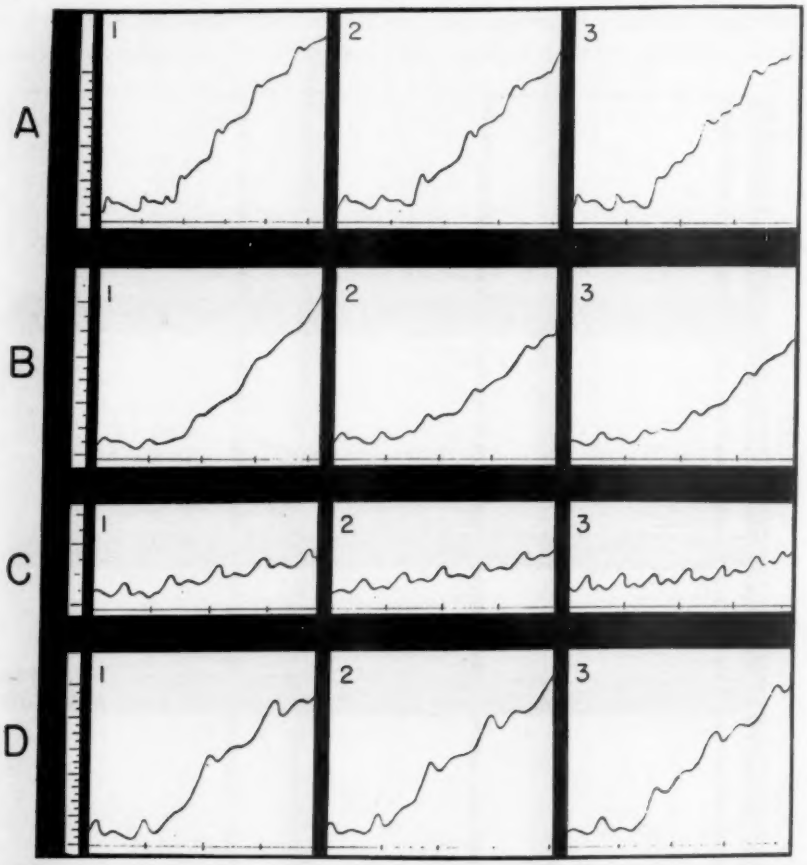

Fig. 2.—Effect of smoking upon blood flow (subject L.S.) in various blood vessel beds at a bath temperature of 32° C., but with the extremity in the plethysmograph reflexly vasodilated. *A*, Blood flow in hand (vol. 430 c.c.): *1*, before, 26.8 c.c.; *2*, during, 22.6 c.c.; *3*, after, 24.8 c.c. *B*, Blood flow in forearm (vol. 475 c.c.) together with hand: *1*, before, 12.6 c.c.; *2*, during, 10.8 c.c.; *3*, after, 12.6 c.c. *C*, Blood flow in forearm alone: *1*, before, 2.4 c.c.; *2*, during, 2.9 c.c.; *3*, after, 2.7 c.c. *D*, Blood flow in foot and adjoining portion of leg (vol. 1250 c.c.); *1*, before, 9.1 c.c.; *2*, during, 9.4 c.c.; *3*, after, 8.7 c.c.

blood flow, or even a slight increase, despite the fact that measurements of flow in the hand alone, or in the forearm plus the hand, obtained during the same procedure, showed definite and significant decreases. Likewise, in the reflexly vasodilated extremity (Table II, Fig. 2), in all cases (four trials) there was no significant decrease in blood flow with

TABLE III

EFFECT OF SMOKING UPON BLOOD FLOW AT A BATH TEMPERATURE OF 45° C.

SUBJECT	HAND			FOREARM-HAND			FOREARM			FOOT-LEG			REMARKS
	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	BEFORE	DURING	AFTER	
L. S.										12.6	12.9	11.7	Normal
										25.5	25.0	22.0	
				28.8	29.2	26.8				18.3	16.4	16.4	
	29.4	30.6	30.5	12.2	13.3	12.2	10.4	9.6		13.6	15.7	17.6	
B. L.	34.4	22.7	36.6										Normal
J. M.	37.6	38.7	38.0							9.8	10.1	9.3	Normal, nonsmoker, didn't inhale
A. R.										9.7	9.7	9.0	Normal
										11.3	9.3	8.7	
M. M.	36.2	32.0		10.6	10.7	9.8	6.8	6.4	6.8				Normal, nonsmoker, didn't inhale
H. C.	30.8	29.0	28.4	9.5	11.1	11.1	7.3	8.6	7.8				Normal
C. R.	19.8	19.8	22.7										Normal
L. M.										8.9	8.0	8.9	Generalized arteriosclerosis
										8.4	10.2	7.7	
										7.6	7.6	7.0	
L. F.	40.8	39.4								9.2	10.3	9.1	Generalized arteriosclerosis
H. M.										13.1	14.5	13.9	Hypertension
A. K.	36.6		33.2							7.9		9.6	Thromboangiitis obliterans of lower extremities
C. S.	43.9	37.6											Thromboangiitis obliterans of lower extremities
O. C.										6.8	7.1	6.5	Hypertension

All figures represent blood flow per min. per 100 c.c. of limb volume. Room temp. 25° to 27° C.

smoking. At a bath temperature of 45° C. (Table III, Fig. 3), a slight increase in flow was observed in one instance and no significant change in two others.

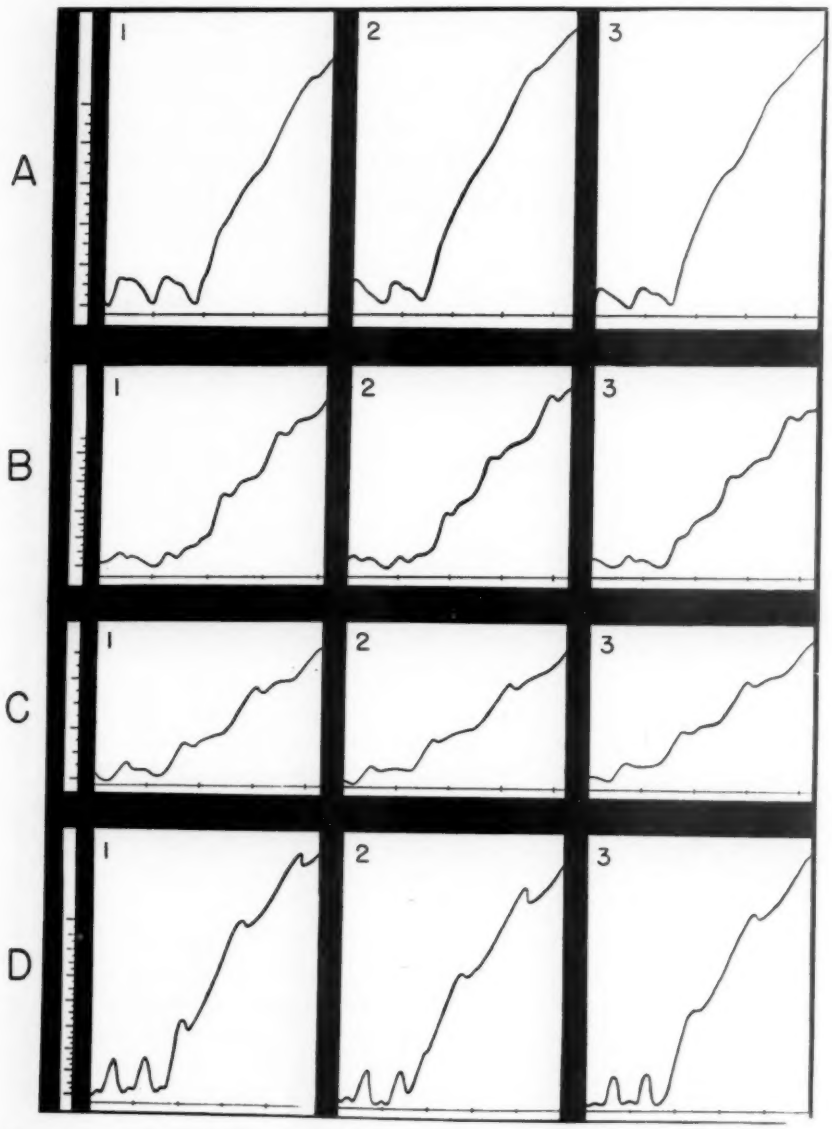

Fig. 3.—Effect of smoking upon blood flow (subject L.S.) in various blood vessel beds at a bath temperature of 45° C. *A*, Blood flow in hand (vol. 456 c.c.): *1*, before, 29.4 c.c.; *2*, during, 30.6 c.c.; *3*, after, 30.5 c.c. *B*, Blood flow in forearm (vol. 530 c.c.) together with hand: *1*, before, 28.8 c.c.; *2*, during, 29.2 c.c.; *3*, after, 26.8 c.c. *C*, Blood flow in forearm (vol. 500 c.c.) alone: *1*, before, 10.4 c.c.; *2*, during, 9.6 c.c.; *3*, after, 9.6 c.c. *D*, Blood flow in foot and adjoining portion of leg (vol. 1380 c.c.): *1*, before, 12.6 c.c.; *2*, during, 12.9 c.c.; *3*, after, 11.7 c.c.

4. *Effect of Smoking Upon Blood Flow in the Foot and Leg.*—In respect to the lower extremity, the foot and at least five inches of the

adjoining portion of the leg were within the plethysmograph, so that blood flow measurements reflected the combined response of the blood vessels in both sites. At a bath temperature of 32° C. (Table I, Fig. 1), in the group of normal subjects a definite decrease was obtained in three instances and a slight effect in one. In the remaining three trials no significant change was observed. In the group of abnormal subjects a slight decrease occurred in four, no effect in seven, and an increase in two. The increase in flow was observed in a patient with hypertension and in one with scleroderma. In the reflexly vasodilated extremity (Table II, Fig. 2) there was no significant change in blood flow (three trials) in either normal or abnormal subjects. At a bath temperature of 45° C. (Table III, Fig. 3), in the normal group there were a definite decrease in four subjects, no effect in two, and an increase in another In the abnormal group there were no effect in two, an increase in four. and a slight decrease in one.

DISCUSSION

It is obvious from an examination of the above data that smoking produced no reduction in total blood flow in the forearm alone under any of the conditions maintained during the experiments. That this was not due to a lack of response on the part of the subject is readily proved by the fact that there was a simultaneous and significant decrease, both in the hand alone and in the forearm and the hand together, at a bath temperature of 32° C. (Table I). On the basis of the observations of Grant and Pearson[10] that skin and subcutaneous tissue form about 50 per cent of the volume of the fingers, and that muscle makes up about 85 per cent of the volume of the forearm, it may be assumed that local blood flow changes in the hand are dependent to a considerable degree upon alterations in the caliber of cutaneous blood vessels, whereas in the forearm the muscle vessels play the predominant role. If these assumptions are correct, and, further, if the muscle of the forearm can be considered representative of similar tissue elsewhere at the periphery (and there is no evidence to the contrary), then the more general statement can tentatively be made that smoking causes constriction of the arteries in the skin, but apparently has little, if any, effect upon those in voluntary muscle. All of the data appear to support such a view. For instance, when vascular changes in the hand were permitted to influence the blood flow measurements obtained from the forearm (i.e., by allowing the blood pressure cuff at the wrist to remain deflated during a forearm blood flow measurement), smoking caused a decrease in flow which disappeared upon inflation of the cuff. In accord with this is the observation that in no instance was the degree of change in the forearm and hand together as great as that in the hand alone. In the studies on the lower extremity, the effect of smoking, at a bath temperature of 32° C., was much less marked than in the hand

under similar conditions; this can be correlated with the fact that a portion of leg, made up principally of muscle, was enclosed in the plethysmograph.

Another point which must be considered is the fact that blood flow through the forearm is to some extent influenced by the state of the blood vessels in the skin, which makes up about 9 per cent of the extremity volume.[10] If we assume that these vessels react in the same way as similarly located arterioles in the hand,* then smoking should constrict them, causing a decrease in the rate of total blood flow. However, since the blood flow in the forearm was not only not diminished, but in some cases even increased slightly, the possibility exists that although some constriction of the blood vessels in the skin may have taken place, it was largely masked by a simultaneous dilatation of the vessels in the muscle. This view is in accord with the observations of other workers that the blood vessels in the muscle and those in the skin respond differently to various stimuli. For instance, Friedlander and her associates,[11] by means of thermocouples, were able to demonstrate that, with such procedures as the production of reflex vasodilatation, paravertebral block, and spinal anesthesia, the skin temperature in human subjects rose significantly while that of the muscle remained unaffected. Further, Grant and Pearson[10] have shown that, in the forearm and leg, minute doses of epinephrine, introduced intravenously or subcutaneously, caused an increase in limb volume and blood flow, while in the digits definite vasoconstriction was produced. Abramson and Ferris[12] have found that with such a stimulus as a pinch, or the performance of a mental task, there was a definite decrease in blood flow in the hand, but no change, or even an increase, in flow through the forearm.

Comparison of the effects of smoking upon blood flow in an extremity under different environmental conditions reveals certain variations in the degree of response elicited. For instance, in the hand, at a bath temperature of 32° C. (equal to average skin temperature), vasoconstriction was generally produced by smoking; with reflex vasodilatation a decreased flow still resulted, but to a relatively small degree. On exposing the hand to a bath temperature of 45° C., smoking generally produced no effect, although in occasional instances a definite vasoconstriction was still observed. The same type of variation with changes in bath temperature was observed in the foot and leg, and in the forearm and hand together. As has been stressed before, smoking produced no decrease in blood flow in the forearm alone, irrespective of the state of the blood vessels.

It would appear from the foregoing that when the blood vessels in the hand are dilated, either reflexly or by the direct application of heat,

*A possible objection to this statement is the fact that there are many arteriovenous shunts in the skin of the fingers which are not present in the skin of the forearm. This anatomic finding may in part explain the differences in response of the forearm and hand.[10]

their responses to smoking are less pronounced than when they are in the natural state of tonus. It is also of interest to note that when the blood flow before smoking, at a bath temperature of 32° C., was small, as was observed in some of the cases in the abnormal group, smoking was relatively ineffective. That this initially low level was due to the presence of excessive vasomotor tonus, and not to organic involvement, is suggested by the fact that on exposing the same extremity to a bath temperature of 45° C. (thus reducing central control over the vessels) normal blood flow measurements for that temperature were generally obtained. It would appear, therefore, that the blood vessels in the skin of the hand do not respond maximally to smoking when they are either excessively dilated or abnormally constricted.

It was noted during the period of smoking that spontaneous vasomotor variations in the hand, as demonstrated by alternate short rises and falls in the baseline (indicating changes in limb volume), were definitely reduced. At the end of the procedure the fluctuations again appeared. That a state of constriction is present during the period of smoking is further suggested by the results obtained in three experiments on the hand in which the constrictor response to such stimuli as a pinch or performing a mental task was observed during the control period and again while the subject was smoking. In every instance the depression of the baseline produced by the stimulus was much less in the period of maximal effect from smoking than in the control period. In other words, the skin vessels in the hand were already in a state of constriction, so that an additional constrictor stimulus was not as effective as when applied to vessels in a normal state of tonus.

An examination of the results obtained in the group of patients suffering from peripheral vascular disease reveals that, as a rule, the response to smoking on the part of these subjects was less marked than in the control group. Of special interest were the reactions of the patients with hypertension; of the thirteen trials, a slight decrease in blood flow occurred in two, no effect in four, and an increase in seven. The increase took place in the hand in two instances, in the forearm and hand together in two, in the forearm alone in one, and in the foot and leg in two.

SUMMARY

By means of plethysmographic studies, the effect of smoking on peripheral blood flow was observed in a series of normal subjects and in a series of patients suffering from various peripheral vascular disorders. In most instances measurements of blood flow were obtained in two extremities simultaneously.

It was found that a maximal response to smoking was elicited only in an extremity in which the blood vessels were neither excessively dilated nor constricted. In the hand, which is made up largely of skin containing many arteriovenous shunts, smoking produced the greatest decrease

in blood flow. In the foot and adjoining portion of the leg the changes were in each instance relatively less marked than in the hand. In the forearm, which contains muscle to the extent of 85 per cent of its volume, there was no change in blood flow under any of the experimental conditions.

CONCLUSIONS

Judging from our results, the usual statement that smoking causes a decrease in peripheral blood flow[1, 5, 7] should be modified to indicate that the decrease probably takes place only in the blood vessels of the skin, and not in those of voluntary muscle. It follows, therefore, that the constrictor response to smoking observed in skin vessels of the hand cannot be considered as typical of reactions of blood vessels elsewhere in the body.

We wish to express our appreciation to Mr. Joseph Marrus, Mrs. Robert Senior, and Dr. Meyer Margolis for technical assistance in carrying out the experiments.

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HEART SOUNDS IN YOUNG ADULTS*

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HEART sounds have been recorded by various methods for many years. Although a great deal of information has been obtained by means of the older methods, at times the graphs have presented very difficult problems in interpretation. Lockhart[1] has discussed the outstanding contributions of the earlier methods and has presented a new method which overcomes many of the previous difficulties. His apparatus, called the stethograph, was used in our study.

Before records can be fully interpreted, normal standards need to be established. Reports in the literature have been meager, as far as the stethograph is concerned. Martínez Cañas[2, 3] reported on the use of this method, but the number of normal records studied in his series was small. Horine[4] described the clinical use of the stethograph and published records taken with this instrument. McKee[5, 6] has reported on the heart sounds in normal children and children with rheumatic heart disease. In 90 per cent of her series of 105 normal children she found systolic vibrations which she called murmurs, but she did not regard them as significant.

Our study of the stethograms of 110 medical students was undertaken to determine the characteristics and time relationships of the heart sounds of normal young adults, and the significance of systolic and diastolic vibrations, exclusive of the heart sounds themselves, occurring in the absence of audible murmurs.

PROCEDURE

In order to eliminate extraneous sounds, the stethograms were made in a warm, quiet room, with the subject relaxed and respiration suspended. The recordings were made from the apex area with the patient reclining comfortably in the left lateral position. A microphone bell with an opening 5 cm. in diameter was carefully applied in the correct position, as determined by auscultation, and held with a rubber strap.

One of the standard electrocardiographic leads was recorded simultaneously on the same recording paper. The camera speed was routinely 50 mm. per second, which was found satisfactory, although occasional graphs were recorded at 100 mm. per second.

All of the students studied were apparently in good health; they had had physical examinations in the student health department and the majority had also had roentgenograms of the chest at the time of the physical examination. A careful search for the potential etiologic factors of heart disease was made in all cases, and no student with such a factor, or with objective signs of organic heart disease, was included in the series. Thus the subjects studied were free from organic

*From the Florsheim Foundation for the Study of Heart Disease, and the Department of Medicine, Northwestern University Medical School.
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heart disease, as judged by the criteria of the New York Heart Association.[7] Body habitus, height, and weight were noted. The ages ranged between 20 and 30 years in 105 cases; five of the subjects were between 30 and 35 years of age.

All records were carefully analyzed, and artifacts ruled out. If necessary, the stethogram was repeated. The number of vibrations in each heart sound and the systolic and diastolic vibrations which were separate from the true heart sounds were counted in all records. When vibrations varied from heart cycle to heart cycle, an average was taken.

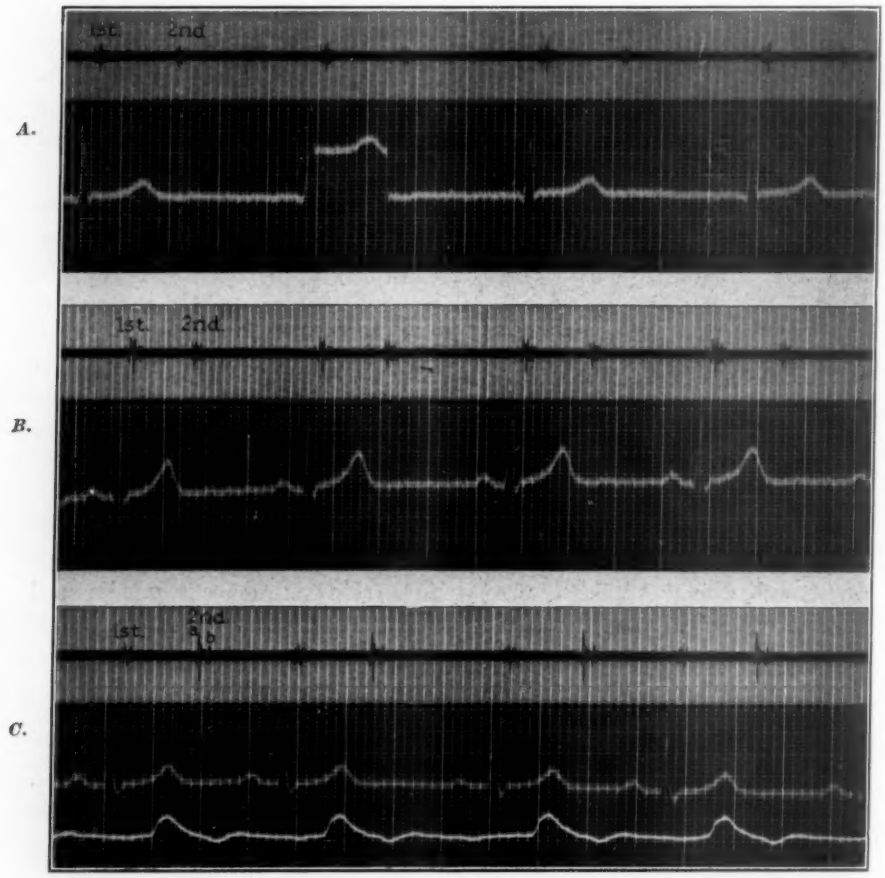

Fig. 1.—Stethograms, with Lead II of the electrocardiogram, showing: *A*, Normal heart sounds. *B*, Normal heart sounds with slight systolic vibration. *C*, Variation of normal sounds, with accentuation and reduplication of the second sound (*a-b*). Electrocardiogram and brachial pulse tracing recorded simultaneously.

RESULTS

All records examined revealed a normal sinus rhythm, with the heart rate varying from 60 to 90 beats per minute.

The first heart sound appeared within 0.04 to 0.06 second after the Q wave, or the first of the initial deflexions of the electrocardiogram. It was composed of 6 to 8 large vibrations in 86.3 per cent of the cases, and of 4 to 10 vibrations in a few isolated instances. The duration of this sound varied from 0.08 to 0.12 second.

The second sound appeared within 0.34 to 0.40 second after the Q wave. It was composed of 4 to 6 vibrations, and its duration was 0.04 to 0.06 second.

The third heart sound was recorded in 33.3 per cent of our series. It occurred 0.48 to 0.52 second after the Q wave, and 0.12 to 0.16 second after the beginning of the second sound. This sound usually had one or two vibrations of rather low amplitude.

The fourth sound was recorded in some instances, but was not constantly present or clearly distinguishable in most of the records examined (Fig. 1).

Sixty-eight records (61.8 per cent) showed vibrations during systole. These varied in number from 4 to 26. Systolic murmurs were audible in ten instances (9 per cent), and examination of the stethograms of these subjects revealed that from 16 to 26 systolic vibrations were present in every record. In the other fifty-eight cases in which there were systolic vibrations and no audible murmur, only twelve records resembled those obtained from the subjects with audible systolic murmurs, i.e., showed 16 to 26 vibrations in systole (Fig. 2).

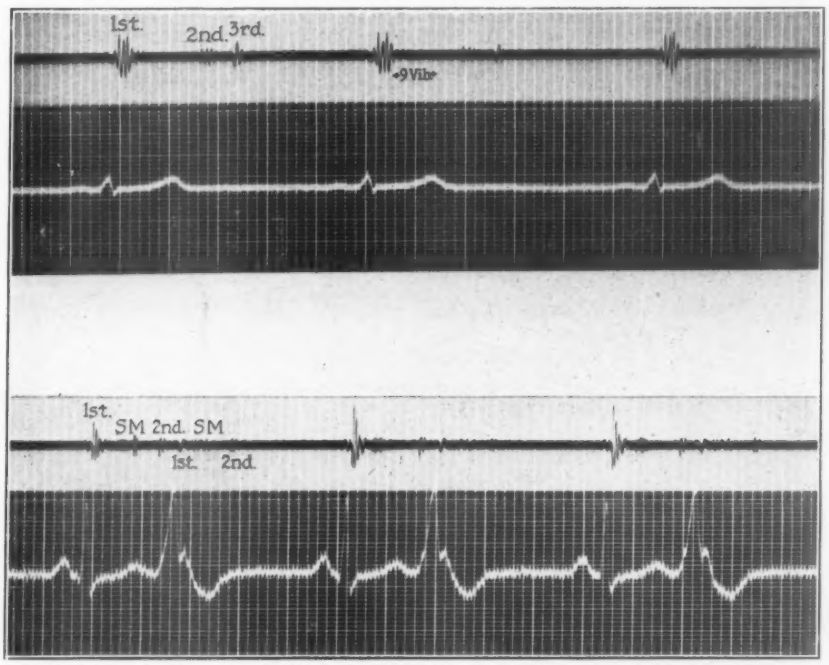

Fig. 2.—Stethograms showing: *A*, Normal heart sounds with nine vibrations following the first heart sound. *B*, Heart sounds from a patient with organic heart disease who had a systolic murmur (*SM*) and rhythmic bigeminy. The first sound of the ectopic beat was inaudible.

A study of body habitus showed that the inaudible systolic vibrations occurred more often in the asthenic type of individual.

Early diastolic vibrations were present in fourteen cases (12.7 per cent). The maximum number of vibrations recorded was 8 to 10. In no instance was a diastolic murmur audible through the stethophones.

It seemed advisable to compare the systolic vibrations found in our series of normal subjects with the records of known organic murmurs. A series of fifty cases of organic heart disease in which there were obvious systolic and diastolic murmurs was studied with the stethograph. These cases will be reported in detail at another time; however, it was ascertained that in the majority of cases an organic systolic or diastolic murmur was represented by 16 to 44 vibrations. Thus it became clear that 20 per cent of the total normal group (medical students) had 16 to 26 systolic vibrations that could not definitely be distinguished from

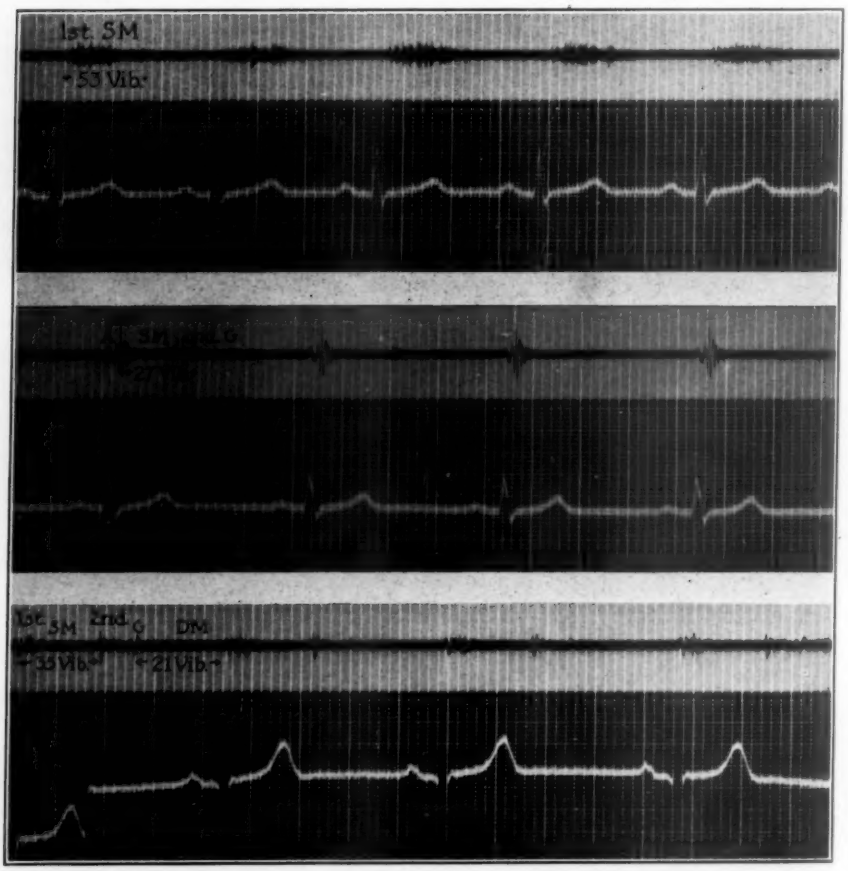

Fig. 3.—Stethograms from patients with organic heart disease showing: *A*, Apical systolic murmur comprising 53 vibrations (*SM*). *B*, Apical systolic murmur comprising 27 vibrations (*SM*) and protodiastolic gallop (*G*). *C*, Apical systolic murmur comprising 35 vibrations (*SM*), diastolic murmur comprising 21 vibrations (*DM*), and protodiastolic gallop (*G*).

the recorded murmurs of organic heart disease. However, the well-defined organic murmurs usually had more vibrations and were of longer duration. Some records of organic systolic murmurs simulated the stethograms showing systolic vibrations which were obtained from normal subjects (Fig. 3).

CONCLUSIONS

The characteristics and time relationships of the heart sounds of 110 normal young adults have been determined by means of the stethograph. The results suggest that, in the interpretation of stethographic records, systolic vibrations should not be regarded as actual murmurs unless there are at least sixteen regular oscillations. Clinical correlation is very important in the interpretation of cardiac sound records; it is not correct to interpret a few irregular oscillations in systole or diastole as a murmur, for they may be due to the impact of the apex against the chest wall, or to other extracardiac factors. Some genuine murmurs may be inaudible in the early stages of their development, but further research is necessary to determine the true significance of recorded vibrations when no sound is audible.

The authors wish to express their appreciation to Dr. J. G. Carr and Dr. A. C. Ivy for their help and constructive criticism in this study.

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THE SIGNIFICANCE OF THE DURATION OF Q_3 WITH RESPECT TO CORONARY DISEASE*

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SINCE 1930, Pardee,[1] Durant,[2] and Wallace[3] have offered various criteria for recognizing QRS changes which they considered highly significant of coronary disease. Their criteria, however, were concerned with amplitude only; they emphasized particularly the importance of a prominent Q_3 in association with a definite Q_2. Primarily because of certain theoretical considerations, it seemed worth while to investigate the duration of Q_3 in a large number of electrocardiograms.

For this purpose 19,000 electrocardiograms recorded from adults were critically examined. At least one-third of the curves had been taken on negro subjects. The duration of Q_3 was measured along the top of the broad base line. Early in the study of these curves and of their related clinical data it became evident that a Q_3 of 0.03 second, or less, in duration was of little importance with respect to coronary disease unless there were also typical changes in the final ventricular deflections.

It was then decided arbitrarily to investigate further all curves of the 19,000 which presented an initial downward deflection in Lead III of duration equal to, or greater than, 0.04 second in at least five consecutive QRS complexes initiated by an impulse of auricular origin. All curves showing right axis deviation, all curves with QRS complexes of 0.11 second, or more, in duration, and all curves having M- or W-shaped complexes in Lead III were excluded.

The 163 electrocardiograms selected on the basis of these criteria were divided into two groups, according to the presence or absence of a Q_2 1 mm. or more in amplitude in at least five consecutive QRS complexes initiated by an impulse of auricular origin. Whether Q_3 was or was not followed by an immediate upward deflection was considered immaterial. This appears to involve the subject of terminology. The initial downward deflection under consideration may be regarded as an S_3 in curves in which there is no preceding Q_3 or R_3, or may be looked upon as a Q_3 in curves in which R_3 is either present or absent. In order to avoid confusion, the notation adopted here is such that the initial downward deflection in Lead III is called a $(QS)_3$ deflection, thus indicating the independence of the presence or absence of an immediate subsequent upward movement.

The group of 163 curves contained 91 examples of the $Q_2(QS)_3$ and 72 of the $R_2(QS)_3$ variety.

*From the Department of Medicine of the School of Medicine, Louisiana State University, and the files of the Heart Station of Charity Hospital of Louisiana, New Orleans, La.
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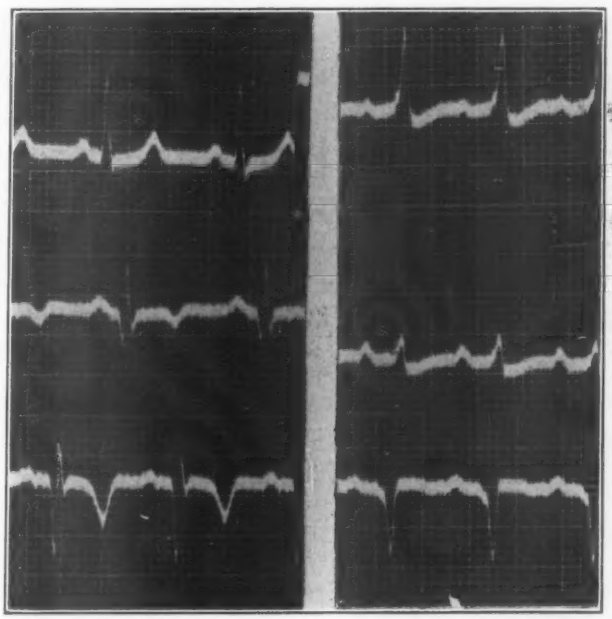
THE $Q_2(QS)_3$ GROUP

In each instance the clinical picture was one of heart disease. The chief findings displayed by the ninety-one patients are presented in Table I. In the compilation of the table, pain associated with exertion, excitement, cold, or heavy eating was considered a necessary part of the coronary disease picture in the absence of unequivocal "coronary" changes in both the initial and final ventricular deflections. Since coronary disease may be present in a patient not having these symptoms and electrocardiographic changes, the value of 82 per cent may be low.



A. *B.*

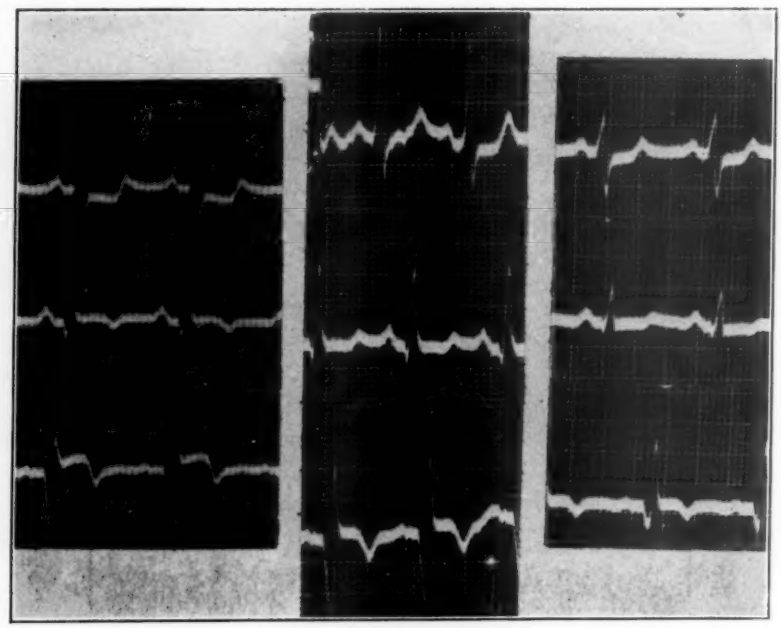
Fig. 1.—*A*, Sample curve of the type selected for the Q_2 $(QS)_3$ group. *B*, Sample curve of the type selected for the R_2 $(QS)_3$ group.

TABLE I

DISTRIBUTION OF 88 PATIENTS IN THE $Q_2(QS)_3$ GROUP ACCORDING TO THE ETIOLOGY OF THEIR HEART DISEASE. (THREE PATIENTS IN THIS GROUP, TWO WITH RHEUMATIC HEART DISEASE AND ONE WITH MYXEDEMA, ARE OMITTED FROM THE TABLE.)

HEART DISEASE	ARTERIOSCLEROTIC	HYPERTENSIVE	SYPHILITIC	TOTAL
Number with acute or subacute cardiac infarction	28	14	1	88
Number with pain caused by coronary disease	21	9	2	
Number without symptoms of coronary disease	2	6	5	
% of the etiological type with coronary disease	96	79	60	
% of $Q_2(QS)_3$ group with coronary disease	54	25	3	82

All of the subjects classified as having arteriosclerotic heart disease were white, and all but three were males. In more than half of the curves in this group, the amplitude of $(QS)_3$ was less than half as great as that of the largest QRS deflection. There was an 80 per cent incidence of abnormal changes in the final ventricular deflections. The most common type of RS-T junction and segment deviation was of the Q_3T_3 variety. One-fourth of these curves displayed a so-called coronary T in one or more leads. Auricular fibrillation was rare.



A. *B.* *C.*

Fig. 2.—Curves *A* and *B* were recorded over a one-year period from a white woman, 49 years of age, and indicate the presence of a large posterior infarct. Curve *C* was recorded from this subject one and one-half weeks after a second (anterolateral) infarct.

THE $R_2(QS)_3$ GROUP

The criteria established for this group were identical to those laid down for the $Q_2(QS)_3$ group, except that there was no Q_2. All but one of the seventy-two subjects presented a clinical picture of heart disease. It was found that twenty-one of the twenty-nine patients in the arteriosclerotic subdivision and eleven of the twenty-four patients in the hypertensive subdivision had, or had previously had, definite clinical manifestations of coronary disease. In the syphilitic subdivision five of the twelve patients presented this picture. There were four additional patients with rheumatic heart disease, one of whom had pain caused by coronary involvement. Of the remaining three patients in the $R_2(QS)_3$ group, one had neurocirculatory asthenia, one anemia, and the third was pregnant.

DISCUSSION

Of unusual interest was the case of a white woman, 49 years of age, in which the diagnosis of hypertensive heart disease, diabetes mellitus, and coronary arteriosclerosis had been established. Her electrocardiograms are shown in Fig. 2. Curves *A* and *B*, which were taken nine months before Curve *C*, indicate the presence of a large infarct in the diaphragmatic wall of the left ventricle. She developed symptoms of acute cardiac infarction one and one-half weeks before Curve *C* was taken and died a few days after this recording. Curve *C* resembles the previous curves in all essential particulars. A marked diminution in amplitude has occurred, however, in both Q_2 and $(QS)_3$. This, together with the changes in the clinical manifestations, was believed to indicate the development of an infarct of the anterior wall of the heart.

Necropsy revealed an old posterior, and a recent anterior, infarct of the inner half of the wall of the left ventricle. A strikingly similar course of events was observed in a case reported by Wilson.[4]

When the records of the $Q_2(QS)_3$ and $R_2(QS)_3$ groups were considered jointly and those eliminated in which a diagnosis other than acute or subacute cardiac infarct was justified, it was observed that there were five times as many of the related electrocardiograms in the $Q_2(QS)_3$ group as in the $R_2(QS)_3$ group. This observation corroborates the opinion, expressed independently by Durant and Wallace, that the presence of a Q_2 in addition to a prominent Q_3 lends further support to the presumptive diagnosis of coronary disease.

The criteria suggested for the $Q_2(QS)_3$ group appear to have an advantage over those offered by Durant, for they enable one to select, without loss of specificity, all of the curves which would be included on the basis of his most rigid QRS criteria, plus at least as many more additional curves.

SUMMARY AND CONCLUSIONS

1. A critical examination of 19,000 electrocardiograms led to the establishment of new criteria for recognizing QRS changes which are highly significant with respect to coronary disease.

2. Emphasis is placed upon a broad $(QS)_3$ of large amplitude which subsequently undergoes a sharp diminution in amplitude. This change alone is thought to be indicative of anterior infarction when it occurs in a patient who has already had infarction of the posterior wall of the heart.

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THE TREATMENT OF OCCLUSIVE ARTERIAL DISEASE OF THE LEGS BY MEANS OF THE SANDERS VASOCILLATOR (SANDERS BED)

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IN 1936, Sanders[1] described a motorized oscillating bed for the treatment of cardiac and vascular diseases. This bed has recently been described and accepted by the Council on Physiotherapy of the American Medical Association[2] under the name "Sanders vasocillator." In brief, it consists of an ordinary hospital bed attached to a special cradle, so that the bed can be rocked on a transverse axis across its midportion after the manner of a child's seesaw. By means of an electric motor the bed is tipped on this transverse axis continuously, so that the head of the bed is alternately raised and lowered through an arc of approximately 60 degrees. The period of oscillation can be adjusted to take from one to seven minutes for a complete cycle. It is possible to change the midposition of the bed through a small arc, so that, in the extreme positions, the head of the bed may be higher and the foot lower at the end of the cycle, or vice versa. The head and foot of the bed are hinged so that either can be raised, and the patient made to lie in the semirecumbent position with the thighs and knees partially flexed.

In cases of peripheral vascular diseases the therapeutic principle of this bed is simply the old principle of postural exercises, except that the changes in posture can be carried out for long periods without effort on the part of the patient and with a steady, continuous rhythm.

Sheard has devised a bed on the same principle, but with a different type of mechanism. The foot of the bed is raised and lowered through a fixed arc more rapidly than in the case of the Sanders vasocillator, but intermittently, the movement stopping at the maximal elevation and maximal dependency for certain periods. The period during which the bed is stopped can be varied from a few seconds to several minutes by a simple adjustment. An advantage of Sheard's bed is that the periods of elevation or dependency can be more easily varied. It possesses the disadvantage that patients are more conscious of the intermittent than of the continuous motion.

This report is based on observations of eighty-eight cases of occlusive arterial disease of the legs in which the patients were treated with these beds. The eighty-eight cases consist of thirty-eight cases of arteriosclerosis obliterans without diabetes mellitus, sixteen cases of arteriosclerosis obliterans with diabetes mellitus, thirty-one cases of thromboangiitis

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obliterans, two cases of embolic arterial occlusion, and one case of traumatic arterial occlusion. No difference could be observed in the effect of the bed in cases of different types of arterial lesions in which the symptoms and degree of arterial insufficiency were roughly the same.

In using the beds it was found that it was important to have the patient in a comfortable position, and to secure enough flexion of the thighs and knees so that when the head of the bed was at its maximal elevation the patient's body did not slip toward the foot of the bed. It also was found that adjustments of the bed were usually necessary for each patient, that it was usually advisable to run the Sanders bed at a rather rapid speed (cycle of two minutes), and that it was desirable to have the feet of the patient just become blanched when they were in the elevated position and just develop rubor when they were in the dependent position before the direction of motion changed.

PHYSIOLOGIC EFFECTS

The most obvious physiologic effect was the change in the color of the skin during the cycle of oscillation, which indicates that there were alternate filling and emptying of the capillaries in the skin of the feet and toes. Studies of the skin temperature were carried out on six patients before and after treatment with the bed (Table I). In general, it can be said that there was only a minor increase in the skin temperature, although this depended upon the degree of arterial obstruction in the extremity. The elevation in skin temperature was less than that produced by other vasodilating agents, such as typhoid vaccine and ethyl alcohol, in the same cases. In a series of cases oscillometric readings were taken before and after treatment with the bed. There was usually, but not always, a slight increase in these readings; this was less marked, or absent, in those cases in which the patients had severe degrees of arterial obstruction. One interesting effect of the bed was that the majority of the patients became rather sleepy after they had been on it for a comparatively short time, the oscillating movement apparently having a definite soporific effect. Since ordinary sleep causes vasodilatation, sleep may have been partly responsible for the rise in skin temperature.

IMMEDIATE EFFECT ON PAIN

On the basis of the symptoms and clinical observations the eighty-eight cases were divided roughly into four groups. Group 1 included sixteen cases in which intermittent claudication was the only symptom. Group 2 included thirteen cases in which pain occurred in the digits or feet while the patients were at rest (pretrophic pain). There was no evidence of ulceration, gangrene, or ischemic neuritis in this group of cases. Group 3 was composed of fifteen cases in which the patients had pain which was characteristic of ischemic neuritis. There was no evidence of ulceration

or gangrene in any of the cases in this group. In group 4 there were forty-four cases in which the patients had ischemic ulcers or gangrene and severe pain in the region of these lesions.

TABLE I

RISE OF SKIN TEMPERATURE AFTER TREATMENT WITH SANDERS BED FOR 1.5 TO 2 HOURS

	CASE 1		CASE 2		CASE 3		CASE 4		CASE 5		CASE 6	
	LEFT FOOT	RIGHT FOOT	LEFT FOOT	RIGHT FOOT	LEFT FOOT	RIGHT FOOT	LEFT FOOT	RIGHT FOOT	LEFT FOOT	RIGHT FOOT	LEFT FOOT	RIGHT FOOT
Average rise in temperature of skin of toes, degrees C.	2.2	1.5	2.0	2.7	0.1	1.1	2.0		3.8	3.3	1.0	1.1
Average maximum temperature of skin of toes, degrees C.	32.5	32.3	33.0	33.7	29.7	28.5	31.2		32.4	32.2	29.7	28.6

The most striking effect of treatment with the bed was the relief of pretrophic pain, the pain of ischemic neuritis, and the pain which was associated with ulceration and gangrene. In twelve of the thirteen cases in group 2 the patients obtained complete relief from pain while they were on the bed. Similarly, of the fifteen patients in group 3, nine obtained complete relief of neuritic pain while they were on the bed, and four more obtained partial relief. In thirty-two of the forty-four cases in group 4 the patients obtained complete relief from pain while they were on the bed. A striking example was that of a woman who had hypertensive heart disease and auricular fibrillation. She had had arterial emboli in both legs; these emboli had resulted in complete arterial obstruction at a point just below the right knee, and progressive gangrene of the entire foot and leg developed. She suffered from severe pain in the region proximal to the upper margin of the gangrene. The pain could not be controlled by the administration of morphine, but she secured complete relief from pain while she was on the oscillating bed. Several times the bed was stopped in various positions, but each time the pain returned in a few minutes, and it was necessary to start the oscillation of the bed again in order to relieve the patient. In practically all instances in which relief from pain was obtained, the pain recurred after the patients were taken off the bed during the early periods of treatment. Many patients stated that while they were on the bed they were able to sleep without the help of drugs for the first time in several weeks.

RESULTS OF PROLONGED TREATMENT

The persistent effects of the treatment on the symptoms and manifestations of arterial insufficiency were somewhat difficult to evaluate. Of the

eighty-eight patients, some were treated only one hour a day for comparatively short periods, whereas others were treated more intensively for long periods, and still others were kept on the bed practically continuously for several days or weeks. Some of the eighty-eight patients were given other types of treatment during the period that they were being treated with the bed. In trying to evaluate the results an attempt was made to be conservative. Most of the patients were not ambulatory, and some of the improvement noted may have been simply the result of rest in bed, warm environmental temperatures, and the natural tendency of the circulation of the extremities to improve in the absence of further episodes of arterial occlusion.

Group 1.—In eight of the sixteen cases in group 1 a definite improvement was noted, but it was felt that this was due to other types of treatment. In general, there appeared to be no definite improvement with respect to intermittent claudication following treatment with the bed.

Group 2.—In eleven of the thirteen cases in this group relief of pain persisted after the treatment was discontinued. In five of these eleven cases the patients were treated only with the bed. The other six patients received other types of treatment which may well have produced the same results if the bed had not been used. However, it is not certain that this would have occurred.

Group 3.—In nine of the fifteen cases in group 3 relief of pain persisted after the treatment was discontinued. In seven of these nine cases the patients were treated only with the bed.

Group 4.—In twenty-two of the forty-four cases in group 4 the ulcers or gangrene healed and the patients obtained complete and persistent relief from pain. In twelve of the twenty-two cases (eight cases of arteriosclerosis, two cases of thromboangiitis obliterans, and two cases of arterial embolism) the patients were treated only with the bed, except for the use of bland, warm, foot soaks and warm environmental temperatures. In the other ten cases all of the patients had thromboangiitis obliterans, and, in addition to treatment with the bed, typhoid vaccine was administered intravenously. In these cases the healing of the lesions and relief of pain were probably, although not certainly, due to the injections of foreign protein rather than to the effect of the bed.

COMMENT

In summarizing the effects of treatment in the seventy-two cases in groups 2, 3, and 4, it can be said that persistent good results were obtained in twenty-four, or 33.3 per cent. In these cases the patients were treated only with the bed. Persistent good results also were obtained in eighteen other cases but in these cases the results may well have been due to the other types of treatment which were given simultaneously. No persistent benefit was obtained in thirty, or 41.7 per cent, of the seventy-two cases, regardless of whether the bed was used alone or in conjunction

with other types of treatment. In this paper we have used the term "persistent good results" to mean relief from pain and healing of ulcerative or gangrenous lesions which persisted for a period of at least six months after the treatment was stopped. It is well known that patients with occlusive arterial diseases of the legs may have relapses due to occlusion of other arteries.

A few other observations are worth mentioning. In five of seven cases of comparatively recent acute arterial occlusion and marked ischemia, there was definite evidence of improvement of the circulation after a few days of intensive treatment. In one of these cases the patient was a man who had had thromboangiitis obliterans for ten years. He entered the hospital two days after the occurrence of acute arterial occlusion. He had moderately severe pain in his right foot. There was a definite reduction of sense perception in the distal half of the foot, which was cold and shrunken. The foot became completely blanched on elevation, and on dependency after elevation the color did not return in the skin of the toes until two minutes and fifteen seconds had elapsed. He was treated with the bed alone for twenty-three out of each twenty-four hours. After four days the color returned in the foot forty-five seconds after dependency during the elevation-dependency test. Sense perception returned to normal, and the pain was completely and permanently relieved.

It is interesting to note that, when the bed was satisfactorily adjusted, we did not observe any case in which the pain became worse while the patient was on the bed, and untoward effects from treatment on the bed were noted in only one case. In this case the patient had thromboangiitis with gangrene of a toe and beginning gangrene of the distal portion of the foot. After treatment on the bed had been continued for two days, an ascending lymphangitis of the leg developed. We are not certain whether this was due in any way to treatment with the bed. In thirty-four cases it was possible to make some comparison between the effects of treatment with the bed and the effects of treatment with the intermittent suction and pressure machine. Of these thirty-four patients, seven who were unable to tolerate the suction pressure machine because it aggravated their pain obtained relief with the bed. Fourteen other patients felt that they had obtained definite relief from pain while they were on the bed, whereas they had not obtained any relief from pain with suction and pressure. Three patients felt that suction and pressure had produced definite relief from pain, while the bed had not. Nine patients felt that they had been relieved both by suction and pressure and by the bed in an approximately equal degree, and eight patients felt that neither the suction and pressure nor the bed had relieved their pain.

SUMMARY

The following is an attempt to summarize the value of the Sanders bed in the treatment of occlusive arterial diseases of the extremities, based on

the effects observed in the eighty-eight cases. We have found no contraindications to the use of this method of treatment, with the possible exception of the presence of marked infection in association with gangrene. The bed can be used for comparatively short periods, or patients can be kept on it continuously for days or weeks. In comparison with other mechanical methods of treatment of peripheral circulatory diseases, it possesses the advantage of avoiding any constriction of the leg or obstruction to the venous circulation. It can be used in conjunction with vasodilating procedures, such as artificially induced fever, drugs given by mouth, or increased environmental heat. To secure the best effects, it is necessary to vary the position and timing of the cycle in accordance with the needs of the individual patient. This form of treatment produces slight objective improvement in circulation, and slight, but incomplete, vasodilatation. Its most striking therapeutic effect appears to be the immediate relief of pretrophic pain, the pain of ischemic neuritis, and the pain of ulceration and gangrene. Relief of these types of pain is not necessarily maintained when the treatment is discontinued. The bed apparently has minimal, if any, beneficial effects on the pain which causes intermittent claudication. It constitutes a valuable addition to the armamentarium for the treatment of peripheral arterial diseases, but it should not supplant other methods of treatment.

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THE SYNDROME OF SUPERIOR VENA CAVAL OBSTRUCTION

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CLINICAL and pathologic reports of obstruction of the superior vena cava are uncommon. Ehrlich, Ballon, and Graham,[1] in 1933, were able to collect from the entire literature only 309 cases. Minor degrees of compression of the superior vena cava are probably much more common than the comparatively small number of these reports would lead one to believe. A slight compression may cause no symptoms, and the signs may be so meager that either they are disregarded or overlooked entirely. Major obstructions by neighboring mediastinal tumors are probably also not as uncommon as the small number of reports in the literature suggests, because the symptoms of venous obstruction are to a considerable extent masked by more obvious and distressing symptoms, such as dyspnea and dysphagia, caused by pressure on other mediastinal structures. Furthermore, the obstruction is rarely complete, or of sufficiently long duration, because of the nature of the lesion causing it, to necessitate the development of a collateral circulation. On the other hand, occlusion of the superior vena cava without a demonstrable tumor in the mediastinum is rare. Survival, with the development of an adequate collateral circulation, is still more rare.

The following case is reported to illustrate the complete syndrome of occlusion of the superior vena cava, and to demonstrate the value of roentgenographic visualization of the vascular system, of segmental circulation time studies, and of venous pressure measurements in the diagnosis of such an obstruction.

REPORT OF CASE

L. G., a man 30 years of age, first came to the Outpatient Medical Department of the Temple University Hospital because of a buzzing sensation in both his ears. Upon examination, many enlarged subcutaneous veins were seen over the upper half of his body. He entered the Temple University Hospital Jan. 9, 1939. The following history was obtained:

The patient was born in Russia, and as a child had scarlet fever, measles, chicken pox and typhus fever. He came to America at the age of 9 years and had always lived either in Philadelphia or New York City. Ever since adolescence he had worked as a paperhanger. He had been well until 1929, when he was 21 years old. At that time he was in New York City. He felt well and considered himself so until his friends told him that his face and neck were swollen to one and one-half times normal size and that his face had taken on a peculiar, greenish-red (cyanotic?) color. At first he paid no attention to this, but within a week he himself noticed the change, and at the same time he observed that his eyes were becoming very prominent and appeared as if they would pop out of his head. All through the day and night he

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was disturbed by peculiar "machinery-like" noises in his head. This drove him finally to seek medical attention. He entered St. Luke's Hospital, in New York City, Oct. 8, 1929, and was discharged Dec. 24, 1929. During his stay in the hospital he had an intermittent fever with recurrent chills and sweats. Because of his frequent complaints of headache, a spinal puncture was done, and the cerebrospinal fluid was found to be under increased pressure. (The details of the clinical and laboratory studies are not available.) He felt well upon discharge and soon began to notice prominent veins over the upper half of his body. These continued to increase in size.

He regarded himself as well until one month before admission to the Temple University Hospital. At that time he developed a buzzing in his ears. This buzzing was synchronous with the heart beat, was aggravated by emotional upsets, exercise, and the assumption of the upright position, and was improved by rest and lying down. He stated that he often had occipital headaches, that his eyes frequently became bloodshot, and that he developed diplopia when he hyperextended his head.

Physical examination revealed a well-built, well-nourished young man. There was nothing of note in the entire examination, including the ear drums, except for the presence of the large subcutaneous veins. The heart was entirely normal in size, shape, and position, as judged by physical and fluoroscopic examination; the sounds were regular and normal. The electrocardiogram was normal. There was no evidence of a mediastinal tumor. The liver and spleen were not palpable. There was no fluid in the abdomen and no edema of the legs.

The veins of the head, particularly the postauricular, were engorged and enlarged, even in the standing position. The neck veins were likewise enlarged and distended with blood. There were numerous tortuous, dilated, overfilled veins in both the upper extremities, on the anterior and lateral chest walls, and over the abdomen. Particularly prominent were the lateral thoracic veins on both sides. There were no prominent veins over the back or in the lower extremities. It could be easily demonstrated that the lateral thoracic veins emptied caudally into the superficial epigastric veins. This was true in the recumbent position even when the pelvis was elevated by one pillow.

The venous pressure in both upper extremities was measured by the direct von Tabora and Moritz method. The pressure in the right arm, taken in the antecubital vein in the supine position, with the arm abducted to forty-five degrees, and with the zero point adjusted to two and one-half inches dorsal to the angle of Louis,[2] was 17.4 cm. of saline; in the left arm it was 19.8 cm. of saline. These pressures could be raised to 22.5 and 28 cm., respectively, by compressing the thoracic or abdominal veins on the homolateral sides, indicating a definite connection between the veins of the arms and those of the thorax and abdomen. The saccharine time, according to the method of Hitzig, was 32 seconds in the left arm, and 22.4 seconds in the right. These times could be prolonged to a variable extent by exerting more or less pressure on the veins of the thorax and abdomen on the homolateral sides. This indicated that the increase in circulation time was due to the fact that the returning venous blood had to traverse an abnormally long course, rather than to cardiac failure. The venous pressure in the legs was 8.5 cm. of saline.

The presence of prominent veins over the upper half of the body with venous hypertension limited to this area and of retrograde flow of blood in the thoracic and abdominal veins, together with the fact that both the venous pressure and the circulation time could be increased by compressing the thoracic or abdominal veins, established the diagnosis of complete obstruction of the superior vena cava, or of both innominate veins, with or without obstruction of the immediate tributaries.

It was decided to attempt to follow the circulation of the blood by means of some substance which the patient could sense. Five c.c. of a mixture of equal parts of a

20 per cent magnesium sulfate and a 10 per cent calcium gluconate solution were injected rapidly into the left antecubital vein. The patient felt a creeping and warm sensation, successively, in the left shoulder (one second), left axillary region (two seconds), simultaneously in the left precordial area and left upper quadrant of the abdomen (five seconds), in the left lower quadrant of the abdomen (six seconds), heel (eight seconds), hypogastrium (ten seconds), and epigastrium (eleven seconds). This sequence is correct, but the exact time relationship is probably not accurate because of overlapping in the perception of the sensations. A similar injection in the right antecubital vein produced the same sequence of sensations on the right side of the body. From this sequence of events one would assume that the flow of blood was from the antecubital vein to the axillary and lateral thoracic; part then went to the intercostals and internal mammary, and part to the superficial epigastric, femoral, iliac, and inferior vena cava or azygos. No adequate explanation for the sensation in the heel can be given. These tests were repeated several times, and

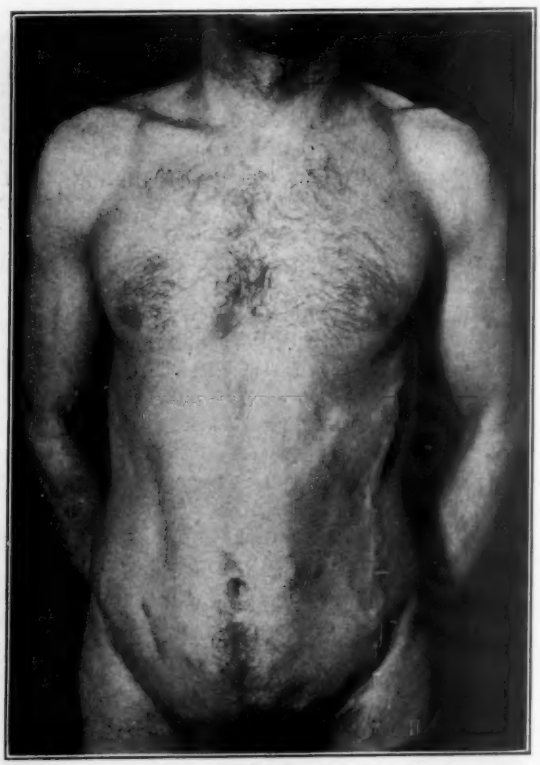

Fig. 1.—Photograph of the patient, showing the large lateral thoracic and abdominal veins.

each time the patient felt a creeping and warm sensation in the heel at approximately the same interval and in the same sequence. No sensation was perceived in the face or neck. As a matter of fact, no adequate explanation can be given for any of the sensations perceived, because these results differ fundamentally from those ordinarily obtained. Clinical circulation-time studies depend upon the transportation of a foreign substance to some special sense organ, whereas in this instance the passage of the foreign body was detected by the patient while it was still in the veins. There are apparently only two possible explanations for this. Because of the venous hypertension, the foreign substance may have diffused through the veins to

the skin. This seems very unlikely. The other explanation is that the veins may have acted as receptor end organs. The only reference to this possibility that I could find was in the monograph by Franklin.[3] Further studies on this question are contemplated.

It was decided to attempt to visualize the abnormal venous communications radiologically. Diodrast was injected into one of the large antecubital veins by means of a large 16-gauge needle, with the arm extended above the head. This injection was completed as rapidly as possible, and two stereoscopic roentgenograms were made on one day in the right anterior oblique position, and on another day in the anteroposterior position, in each instance two and six seconds, respectively, after the beginning of the injection. On the first day 40 c.c. of a 35 per cent solution of diodrast were used, and on the second day, 35 c.c.

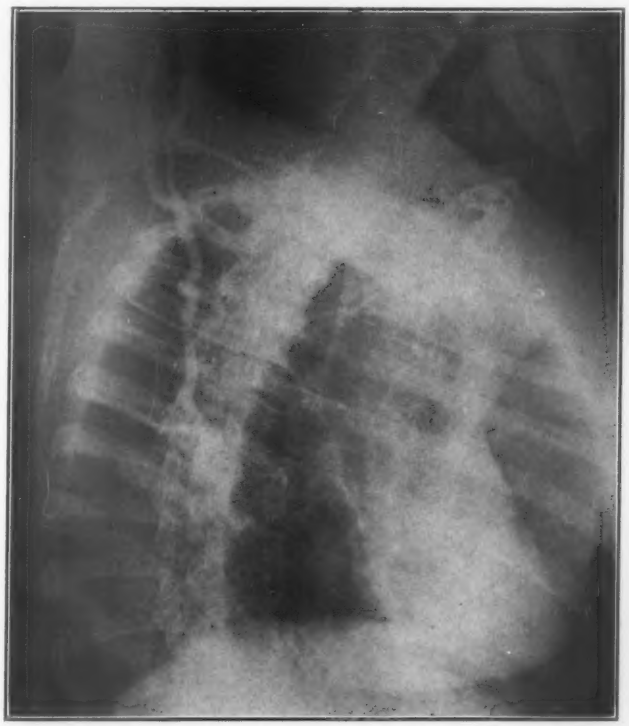

Fig. 2.—Right anterior oblique view, visualizing the veins with diodrast.

Dr. R. P. Meader of the department of radiology of Temple University Hospital interpreted the films. The following is an excerpt from his report:

Right anterior oblique view: "It is probable that the three veins draining the right arm are the cephalic, brachial, and basilic. Anastomoses distal to the point of visualization probably account for the fact that all three are visible. The junction of the basilic and brachial veins, forming the axillary vein, is visualized, but the axillary vein is not visible proximal to the region of the second rib. Instead, there appears to be a definite connection between the junction of the basilic and brachial veins and the lateral thoracic, forming the enlarged superficial vein which is so tortuous down the lateral aspect of the thorax. This continues into the thoracoepigastric, which communicates with the superficial epigastric over the abdomen. The thoracoepigastric vein appears to drain into the intercostal vein on the right

which lies immediately beneath the sixth rib. This is the only one of the intercostals which seems to be connected with this superficial vein.

"The cephalic vein is visualized crossing the right clavicle and proceeding mesially between the clavicle and the first rib. As stated above, the junction of this cephalic vein with the axillary is not clearly seen. Communicating with the continuance of the cephalic vein near the anterior chest wall and proceeding caudally along the axis of the spine, there is a pair of veins which appear to be venae comitantes and are probably the internal mammary veins with an artery between them. These connect with the upper intercostal veins, some of which are well visualized."

Anteroposterior view: "Although the clinician has not stated into which vein the material was injected at this examination, he probably did not use the same antecubital vein as before. This is thought to be true because there is no evidence of visualization of the cephalic or subclavian vein, or of the venae comitantes which were previously regarded as the internal mammary veins.

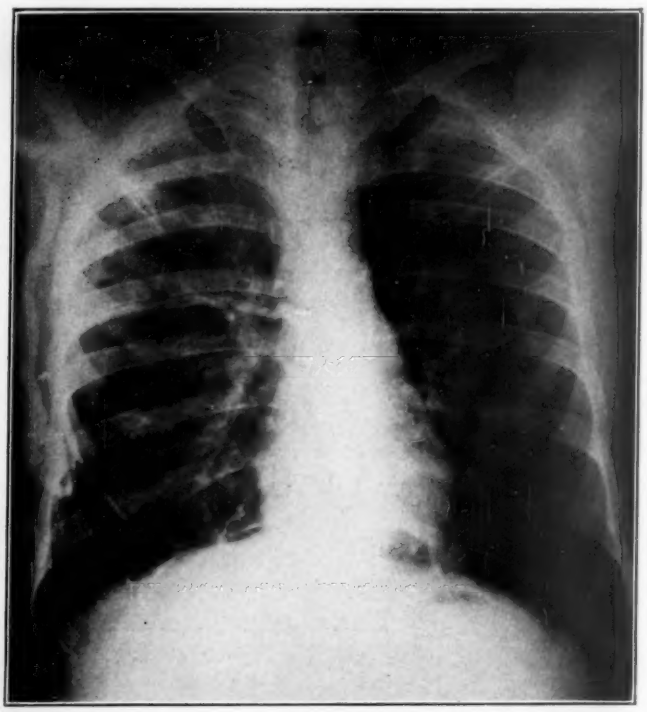

Fig. 3.—Anteroposterior view, visualizing the veins with diodrast and demonstrating the absence of a mediastinal lesion.

"These posteroanterior roentgenograms, which were made two and six seconds, respectively, after the beginning of the injection of the diodrast, show what appears to be the brachial vein emptying into the lateral thoracic vein, which then proceeds in a tortuous fashion down the lateral aspect of the thorax. A branch of this lateral thoracic seems to penetrate the chest wall under the sixth rib in the anterior axillary line and to proceed posteriorly in the region of the sixth intercostal vein. It may be that a branch of this vein also goes anteriorly along the sixth rib, but I believe that the other, smaller veins which are visualized over the lower thoracic wall are probably superficial to the chest wall."

DISCUSSION

The superior vena cava may be partly or totally obstructed, with or without thrombosis, by any mass in the mediastinum. It may also be obstructed by a foreign body or a thrombus. The commonest causes of obstruction are aneurysm of the aorta and malignant tumors. The rarest cause is thrombosis. The following outline enumerates the various causes for superior vena caval obstruction.

1. Aneurysm of the aorta: This may compress the vena cava or may actually rupture into it. The characteristic manifestations of rupture include not only the suddenness of the onset, but also the development of a new, continuous murmur and pulsations in recently enlarged veins of the upper half of the body.[4]
2. Mediastinal tumors
   a. Lymph node enlargement: metastatic carcinoma, leucemia, Hodgkin's disease, inflammatory hyperplasia (syphilis, tuberculosis, granulomata, nonspecific)
   b. Thymus gland enlargement
   c. Thyroid gland enlargement
3. Mediastinitis
4. Pericarditis, with or without effusion
5. Cysts
6. Trauma, due to hemorrhage
7. Thrombosis

Thrombosis of the superior vena cava is also the rarest of all venous thromboses. In an exhaustive review of the literature, Ochsner and Dixon[5] found reports of 120 cases. In not all of these was the diagnosis definitely proved. Of these 120 cases, external compression was the cause in 35 (29.1 per cent); mediastinitis in 28 (23.3 per cent); the cause was either unknown or not stated in 13 (10.8 per cent); and phlebitis was the underlying lesion in 44 (36.6 per cent). Of the 44 cases of phlebitis, syphilis was the cause in 12, tuberculosis in 4, a pyogenic process in 7, and trauma in 1; 10 of the patients had heart disease, and in 10 cases the phlebitis was of unknown origin. Therefore, only ten cases of idiopathic phlebitis with superior vena caval thrombosis had been reported. Since that time one case of tuberculous phlebitis has been reported by Szour and Berman[6] and one of phlebitis of unknown origin by Blasingame.[7]

In the case reported herein, the presence of venous hypertension in the head, neck, and upper extremities indicated obstruction of the superior vena cava and both innominate veins. The roentgenographic demonstration of obstruction of the axillary veins excluded the possibility that a simple encircling band at the base of the superior vena cava was the cause. The only plausible explanation was thrombosis of the superior vena cava extending into its main tributaries, including the axillary

veins. The old history of fever, chills, and sweats suggested that the thrombosis was of infectious origin. The nature of this infection is entirely conjectural. An interesting report of thrombosis of the superior vena cava following influenza was reported by Strauss.[8] This is the twenty- fifth case of superior vena caval thrombosis not due to a mediastinal tumor.

The development of a collateral circulation depends on the site of occlusion of the superior vena cava, i.e., whether it is above or below the azygos vein.

Carlson's[9] experiments on dogs showed that when the occlusion is above the azygos, the superficial veins show the following anastomoses. The axillary unite with the thoracoepigastric to join the plexus over the thorax and abdomen. The veins of the neck anastomose with those of the thorax and empty into the intercostal veins. They also communicate with the superficial epigastric and the superior and inferior epigastric, to unite with the femorals and the external iliac.

The deep veins go from the internal mammary to the intercostals, to the anterior mediastinal, and to the superficial epigastric. There is, furthermore, an anterior and posterior plexus of mediastinal and pericardial veins which empty into the subphrenic and the tributaries of the inferior vena cava. There is also a connection above, through the vertebral column, with the dural sinus and the vertebral veins, and below with the intervertebral and intercostal veins, the deep dorsal veins of the back, the posterior rami of the intercostal veins, and the descending branches of the transverse cervical and scapular veins.

The lumbar veins join the abdominal and suprarenal and the superficial and deep veins of the back; some of them empty into the azygos.

The superficial intercostal and the other intercostals join the accessory hemiazygos and azygos veins.

In this type, the azygos vein, with its tributaries, is greatly enlarged, and becomes the principal channel through which the blood returns to the heart.

When the occlusion is below the azygos, the superficial veins are prominent over the abdomen and thorax. The deep veins go from the internal mammary to the superior and inferior epigastric, to the external iliac veins. There is a rich anterior and posterior mediastinal and pericardial plexus. The vertebral venous plexus is extensively developed; in particular, the internal and the deep collaterals of the back are present.

To summarize Carlson's conclusions, when the occlusion is above the opening of the azygos veins, the azygos vein and its tributaries form the chief channel for the return flow of blood from the upper part of the body to the heart. The lower abdominal collateral veins are relatively unimportant. In the second type, when the occlusion is below the opening of the azygos vein, the superficial and deep abdominal vessels and vertebral plexus are of much greater importance. All of the blood returns to the heart through the inferior vena cava.

In addition to the above collaterals, one must also, according to Ochsner and Dixon,[5] consider the anastomoses between the esophageal and gastric coronary veins and the inferior vena cava.

A beautiful example of the collateral circulation in a case of superior vena caval thrombosis was recently published in the *Archives of Pathology*, and the diagram is reproduced with the kind permission of the author.[7] The lesion was found in the dissection of a cadaver; the body was that of a man 93 years of age, and no history was obtainable.

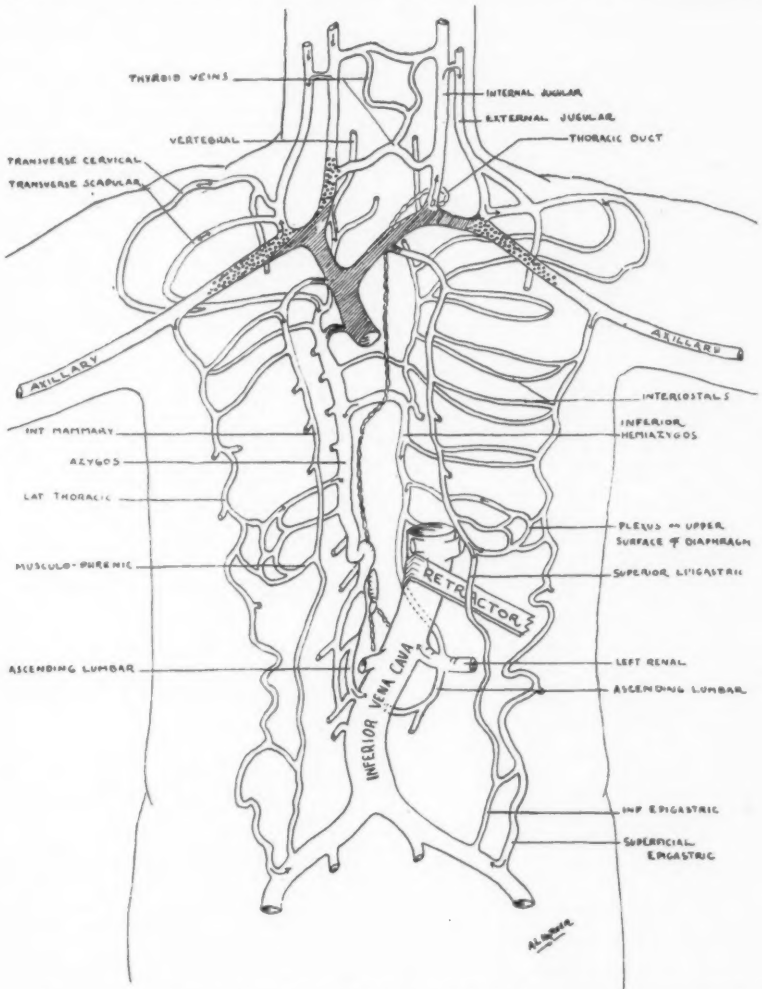

Fig. 4.—Diagram of the collateral circulation. (After Blasingame, with kind permission of the author.)

This case appears to be practically identical with mine, because, as is seen in the diagram, there were complete obstruction of the superior vena cava and the innominate veins and partial obstruction of the axillary veins.

Obstruction of the superior vena cava may occur at any age, but it is most common in the fourth and fifth decades. It occurs with equal frequency in the two sexes. The symptoms depend on the degree of occlusion, the rapidity of its development, and the absence or presence of a collateral circulation. With lesser degrees of obstruction there may be no symptoms, and the diagnosis is made by demonstrating that there is increased venous pressure localized to the upper half of the body. This will be discovered more and more frequently if routine venous pressure measurements are made in all patients suspected of having or known to have mediastinal lesions.[10] In slow, gradual, complete occlusion, there may be no symptoms because the development of the collateral circulation keeps pace with the occlusion. In sudden, complete occlusion, the symptoms caused by congestion of the veins emptying normally into the superior vena cava are dramatic. The superior vena cava returns the blood from the head, face, neck, upper extremities, thoracic walls, and a portion of the upper part of the wall of the abdomen. If the occlusion is sufficient in degree and rapid enough in its development, the patient develops cyanosis and edema of the head, face, neck, and perhaps of the upper portion of the chest and upper extremities. The eyes become prominent, and, if the lesion is sufficiently acute, hemorrhages may occur in the retina and conjunctiva. The intracranial congestion produces peculiar noises throughout the head, disturbs the sensorium, and may cause tinnitus, deafness, papillary edema, somnolence, epistaxis, and, rarely, hemoptysis. The pressure of the cerebrospinal fluid is increased. At the height of the obstruction, the patient sits up and arches his back forward for relief from dyspnea. Fatal edema of the larynx[11] may occur, or death may be due to increased intracranial pressure and anoxemia of the brain. Pleural effusion occurs occasionally. Chylothorax has been produced by experimental occlusion of the superior cava (Blalock, Cunningham, and Robinson[12]) but has not been reported in man. About 75 per cent of the patients die during the acute stage.[5] If the acute stage is survived, the symptomatology will depend upon the amount of collateral circulation. If this is adequate, there may be no symptoms, and the condition is not incompatible with life, as shown in the case of Blasingame's patient, who lived to the age of 93 years. Because of the continuously dilated intracerebral veins, cerebral symptoms, such as headache, tinnitus, vertigo, and even lethargy, are common. These symptoms are usually aggravated by sitting or standing and by exercise, and they are relieved by rest and lying down. Dryness and edema of the skin and dermatoses with itching lesions are occasionally seen in the upper half of the body.

A history of edema and cyanosis of the head, neck, and upper extremities should lead one to suspect superior vena caval obstruction. The presence of venous hypertension in the upper half of the body clinches the diagnosis. The subsequent development of enlargement of

the veins in the upper half of the body, in which the flow is retrograde, and, as shown by means of circulation time and venous pressure studies, with circulatory connections on the homolateral side, completes the demonstration. The symptoms, if any, are due to the lack of adaptability of the skull to this increased pressure. Wagner[13] claims, after studying four cases by the injection method in the human cadaver, that dilatation of the dorsal thoracic veins suggests occlusion, in addition, of the azygos vein. Lian and Abaza[14] state that an increased venous pressure in the upper half of the body, with a normal circulation time, is diagnostic of this condition. As shown in our case, this is not so, and cannot be so if the vena cava is completely occluded. It may be true if the occlusion is not complete, but it is important to remember that the venous pressure in both upper extremities may be elevated by local pulmonary disease, such as tuberculosis. However, in these cases there is no elevation of pressure in the veins of the head or neck unless there is compression of the superior vena cava caused by mediastinal tuberculosis.

The prognosis depends upon the rapidity of development and degree of the obstruction, as well as on the underlying cause. Of those patients with thrombosis of the superior vena cava, 75.9 per cent[5] die in the acute phase. About the same percentage of patients with complete occlusion of the superior vena cava due to mediastinal tumor will die. Partial occlusion is not incompatible with longevity. Once an adequate collateral circulation has formed, the obstruction itself is comparatively unimportant, although most patients will complain of minor, usually cerebral, symptoms. Judging from the experimental work of Carlson,[9] occlusion of the superior vena cava below the azygos vein is more serious than occlusion above the azygos vein and is rarely outlived.

The treatment depends upon the cause. In the acute occlusions caused by mediastinal tumors, roentgentherapy may be tried for radiosensitive lesions, and mediastinotomy for radioresistant lesions. The indication for treatment in cases in which the occlusion is the result of intravascular disease is to relieve the venous pressure in the tributaries of the superior vena cava. This can be done by bleeding, probably best from the jugular veins, and by placing the patient in the proper position. The most favorable position is the recumbent, with the head slightly lowered. Lumbar puncture may be of some help. In the chronic stage the treatment depends upon the severity of the symptoms. Usually no treatment is necessary except occasional sedatives.

CONCLUSION

A case of obstruction, probably caused by infectious thrombosis, of the superior vena cava and its main tributaries is presented. The literature is briefly reviewed, and the diagnostic criteria for this lesion are given.

I am indebted to Dr. Hugo Roesler for suggestions in studying this patient roentgenologically and in the preparation of the manuscript.

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THE COLD-PRESSOR REACTION IN NORMAL SUBJECTS AND IN PATIENTS WITH PRIMARY (ESSENTIAL) AND SECONDARY (RENAL) HYPERTENSION*

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SINCE 1932, when Hines and Brown[1] first reported the response of blood pressure to a standard stimulus of cold, this reaction has been studied by numerous investigators. The results, as indicated in a recent critical review of the literature by Ayman and Goldshine,[2] have not been uniform. The reasons for the discrepancies have been discussed adequately by these writers. In this communication, therefore, the literature on this subject will not be reviewed in detail.

Our interest in this problem was to determine whether the cold-pressor reaction could be used to differentiate between essential hypertension and the secondary forms of hypertension, particularly the type seen in chronic renal disease. For the purpose of evaluating these results statistically, a group of normal subjects was also studied.

METHOD AND MATERIAL

With the exception that we used a recording sphygmomanometer, the method employed was that described by Hines and Brown.[1] The test was carried out with the subject in a comfortable sitting position, except in a few instances in which the patients were recumbent in bed. The blood pressure cuff was applied to one arm, and the other arm was left free. Blood pressure readings were then taken at frequent intervals until a uniform control level was reached. Because of the mechanical slowness of the recording sphygmomanometer, blood pressure readings could not be made at exactly 30- and 60-second intervals after immersion of the hand in water at from 4 to 5° C. In order to keep within the minute limit, therefore, recordings of the blood pressure were taken as rapidly as possible (at least two being obtained), and were discontinued after the hand had been submerged in ice water approximately one minute. Blood pressure recordings were then continued after the hand had been removed from the ice water until the blood pressure had returned to the control level; the time required for the return to the original level was noted.

Eighty-nine subjects were studied; twenty-six were considered as normal individuals, and consisted of interns, laboratory workers, and other members of the usual hospital staff. Eleven subjects had chronic renal disease with or without hypertension, and fifty-two subjects were classified as having essential hypertension.

Following the classification of Hines and Brown, the normal group was divided into two categories, namely, (a) those having a rise of less than 22 mm. Hg systolic and diastolic (16 subjects), who will henceforth be referred to as normals, and (b) those having a rise in systolic or diastolic blood pressure greater than 22 mm. Hg (10 subjects), henceforth referred to as hyperreactor normals.

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RESULTS

Table I gives a comprehensive picture, including a statistical analysis, of the results obtained. In the group of sixteen normal subjects, the average age was 28 years; five were females. The mean rise in blood pressure was 13.9 ± 4.4 mm. Hg, systolic, and 11.8 ± 4.4 mm. Hg, diastolic. In the ten hyperreactor normal subjects, the average age was 27 years; two were females. The mean rise in blood pressure was 37.4 ± 9.2 mm. Hg, systolic, and 25.3 ± 9.1 mm. Hg, diastolic.

Of the eleven subjects with chronic renal disease, the average age was 36 years; four were females. The mean rise in blood pressure was 16.5 ± 7.8 mm. Hg, systolic, and 12.6 ± 6.5 mm. Hg, diastolic.

Of the fifty-two subjects with essential hypertension, the average age was 54 years; thirty-three of the group were females. The mean rise in blood pressure in response to the standard cold stimulus was 35.0 ± 20.0 mm. Hg, systolic, and 21.7 ± 12.2 mm. Hg, diastolic.

Table I also shows that the responses both of the hyperreactor normal subjects and the patients with essential hypertension deviate sufficiently from the normal to be statistically significant. The lack of any appreciable variation from normal in the blood pressure response of patients with nephritis is also evident.

Since only 76 per cent of the patients with essential hypertension gave a hyperreactor response to a standard cold stimulus, an attempt was made to ascertain what factors might influence the degree of pressor reaction in these patients. Thus, as indicated in Table I, the patients with essential hypertension were subdivided into smaller groups according to degree of arteriosclerosis, presence or absence of albuminuria, duration of hypertension, and, finally, according to age. It will be observed that those individuals exhibiting moderate to severe degrees of arteriosclerosis, those having albuminuria (a secondary manifestation in these patients, due to nephrosclerosis), and the aged (61 to 75 years) had an appreciably smaller pressor response to cold than those patients who manifested few or none of these complications, or were younger. However, a considerable number of the older patients with arteriosclerosis gave a hyperreactor response to cold; apparently these factors alone do not account for the lack of a hyperreactor response in some patients with essential hypertension. The duration of the hypertension exerted little or no influence on the degree of pressor response in these patients. This confirms the clinical impression that the duration of hypertension, in general, bears little or no relation to the severity or extent of the secondary lesions.

It was pointed out above that the technique used in this study was fundamentally that employed by Hines and Brown,[1] and later by Ayman and Goldshine.[2] For this reason our results have been compared with theirs (Table II) and show a close agreement.

TABLE I

A STATISTICAL ANALYSIS OF THE RESPONSE OF BLOOD PRESSURE TO A STANDARD COLD STIMULUS IN 89 SUBJECTS

GROUP	NO. OF SUBJECTS	NO. OF TESTS	AVERAGE AGE IN YEARS	SEX		AVERAGE BLOOD PRESSURE		ARITHMETIC MEAN OF RISE IN BLOOD PRESSURE		STANDARD DEVIATION*		PROBABLE ERROR OF MEAN†		$\frac{d}{\sigma_D}$ ‡
				M.	F.	SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC	SYSTOLIC
Normal	16	17	28	11	5	123	77	13.9	11.8	± 4.4	± 4.4	0.72	0.72	0
Hyperreactor Normal	10	12	27	8	2	129	80	37.4	25.3	± 9.2	± 9.1	1.79	1.77	8.22
Nephritic Hypertension	11	16	36	7	4	163	94	16.5	12.6	± 7.8	± 6.5	1.32	1.10	1.17
Essential Hypertension	52	58	54	19	33	209	113	35.0	21.7	±20.0	±12.2	1.73	1.08	7.45
A. Arteriosclerosis 0 to +	35	37	50	11	24	201	108	38.9	22.8	±21.1	±13.0	2.34	1.44	6.91
Arteriosclerosis ++ to ++++	17	21	60	8	9	223	122	28.1	19.8	±15.9	±11.6	2.34	1.71	3.92
B. Albuminuria 0	35	37	39	12	23	200	108	37.1	22.1	±22.3	±13.2	2.47	1.46	5.47
Albuminuria + to +++	13	17	55	7	6	230	129	30.5	21.8	±17.0	±11.1	2.78	1.82	3.91
C. Duration less than 5 years	20	20	54	6	14	206	107	31.1	20.5	±19.1	±13.0	2.88	1.96	3.91
Duration more than 5 years	18	21	53	6	12	221	120	33.7	20.0	±22.0	± 9.1	3.24	1.31	4.03
D. Age 30 to 50 years	18	22	45	4	14	203	118	35.5	20.7	±25.6	±12.9	3.68	1.86	4.32
Age 51 to 60 years	23	25	55	9	14	215	114	38.0	23.5	±19.3	±12.1	2.60	1.63	6.95
Age 61 to 75 years	10	10	68	4	6	213	106	28.4	20.1	±12.8	±13.2	2.73	2.82	3.47

*Standard Deviation: $\sigma = \sqrt{\frac{\Sigma (d^2)}{N}}$,

Where $\Sigma (d^2)$ represents the summation of the squares of the individual deviations from the mean, and N the number of determinations.

†Probable Error of Mean $= 0.6745 \frac{\sigma}{\sqrt{N}}$,

Where σ represents the standard deviation, and N the number of determinations.

‡ $\frac{d}{\sigma_D}$ represents the difference between two means divided by the standard error of the difference. The standard error of the difference σ_D is calculated from the formula, $\sigma_D = \sqrt{\frac{\sigma_1^2}{N_1} + \frac{\sigma_2^2}{N_2}}$

Where σ_1 and σ_2 represent the standard deviations of the two groups and N_1 and N_2 represent the number of determinations in the two groups.

TABLE II

A COMPARISON OF OUR OBSERVATIONS WITH THOSE OF PREVIOUS WORKERS ON THE MEAN RISE OF BLOOD PRESSURE PRODUCED BY A STANDARD COLD STIMULUS

GROUP	HINES AND BROWN		AYMAN AND GOLDSHINE		PRESENT REPORT	
	SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC
Normal	11.4	10.6	10.5	9.0	13.9	11.8
Hyperreactor Normal	29.4	24.5	33.0	17.8	37.4	25.3
Nephritis with and without Hypertension					16.5	12.6
Essential Hypertension						
Preorganic	47.2	34.3				
Organic	34.4	25.4				
All Cases			33.5	19.0	35.0	21.7

DISCUSSION

As stated at the outset, our prime interest in this problem was to determine whether or not the cold-pressor test could be used to differentiate between essential hypertension and hypertension due to chronic renal disease. During the course of this work, Alam and Smirk[3] reported their studies on this subject, showing that, unlike most patients with essential hypertension, patients with nephritic hypertension do not exhibit a pressor response to cold. Our results are in agreement with theirs. Our patients with renal hypertension, however, had an average rise, in both systolic and diastolic blood pressure, slightly higher than in normal subjects, whereas those of Alam and Smirk gave a lower response.

No specific mention was made above of the time required for the blood pressure to return to the control level after removal of the hand from the ice water. Our observations in this respect agree with those of previous writers. Whereas the blood pressure returns to the control level in approximately one minute in normal subjects, this interval may be prolonged to from two to ten minutes in hyperreactor normals and in patients with essential hypertension. Patients with nephritic hypertension are similar to normal subjects in this respect.

SUMMARY

The blood pressure responses to a standard cold stimulus, using a recording sphygmomanometer, in a group of 89 persons, comprising normal subjects, hyperreactor normal subjects, patients with nephritis with and without hypertension, and patients with essential hypertension, are reported and studied statistically.

Thirty-nine per cent of the normal subjects and 76 per cent of the patients with essential hypertension gave a hyperreactor response to cold.

The influence on the cold-pressor reaction of such factors as arteriosclerosis, albuminuria, duration of hypertension, and age of the patients with essential hypertension is discussed.

The blood pressure response to cold in patients with chronic nephritis is similar to that of normal subjects who are not hyperreactors. A hyperreactor response, therefore, in a patient with increased arterial pressure would exclude the possibility of hypertension due to chronic renal disease, but the converse is not true.

Grateful recognition is given to Dr. Robert T. Garrett, of Southampton, Long Island, N. Y., for his aid during the earlier part of these experiments.

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THE CLINICAL SIGNIFICANCE OF RIGHT AXIS DEVIATION IN THE ELECTROCARDIOGRAM

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IN SPITE of the crudeness of the estimation of the electrical axis of the heart by means of the electrocardiogram, significant deviations from the usual normal limits have a clinical value which is not sufficiently appreciated. The scarcity of practical information in the literature concerning the limits of the normal electrical axis and the meaning of abnormal degrees of axis deviation is surprising to those of us who are engaged in clinical electrocardiography. This applies particularly to right axis deviation, about which there exists no adequate clinical study, so far as we are aware.* The purpose of this report is to supply this need and thereby to increase the accuracy of differential diagnosis.

MATERIAL

The basis of this report consists of electrocardiograms of 200 individuals, aged 5 years, or more, showing right axis deviation of more than +90° without low voltage or bundle branch block, but unselected in so far as the clinical diagnosis was concerned. These 200 cases were found among the records of approximately 6000 (3%±) individuals who had had electrocardiograms at the Massachusetts General Hospital. The electrical axis was estimated in degrees by the graphic method to be referred to below, i.e., Einthoven's triangle, as presented by Carter, Richter, and Greene.[2] All tracings having low voltage (maximum height of the QRS complex 5 millivolts, or less) in the standard leads were eliminated because of the unreliability of axis determinations in such instances. Electrocardiograms showing bundle branch, i.e., intraventricular, block were also excluded. Because of the natural tendency to right axis deviation in infants and young children, no patient under 5 years of age was included in this study, and all but five patients were over 10 years of age. Each case record was carefully reviewed, and if there was any doubt as to the cardiac diagnosis, the case was excluded.

As an adjunct to the above material it seemed worth while to evaluate right axis deviation in regard to cor pulmonale, and to the three most common types of congenital heart disease, i.e., the tetralogy of Fallot, interventricular septal defect, and patent ductus arteriosus. Consequently, the electrical axis was estimated in a separate group of such cases if the clinical diagnosis seemed unquestionable.

GENERAL CONSIDERATIONS

At the outset it should be realized that the determination of the electrical axis of the heart by the electrocardiogram is, at best, only a rough

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*Recently Moia[1] has published a detailed study of the electrocardiographic types of right axis deviation in 128 patients, but his paper does not concern itself with the clinical significance of right axis deviation in general.

measurement. This is so because the classical electrocardiogram records the differences in potential produced by the contracting heart muscle in one plane only, whereas actually, since the heart is a solid body, these electrical forces are taking place in many different planes. It is not our purpose to discuss the electrophysical and mathematical concepts upon which the determination of the electrical axis of the heart by the electrocardiogram is based. A review of this material can be found in the report by Prodger and Davis.[3] A summary of the existing factual data and theoretical concepts in so far as they apply to the practical aspects of axis deviation, however, is desirable as a background for the material to be presented subsequently.

The electrical axis as determined by the electrocardiogram can be expressed in one of two ways, either in terms of an angle with the horizontal, or by means of an index. The former was originally suggested by Einthoven, and later simplified for practical application by Carter, Richter, and Greene[2] to a graphic method based on Einthoven's equilateral triangle. Formulas for expressing the electrical axis in terms of an index have been presented by Lewis[4] and White and Bock.[5] There is some difference of opinion regarding the normal limits of the electrical axis. When the angle is employed, both 0° and −10° on the one hand, and +90° and +100° on the other, have been considered the upper boundaries for left and right axis deviation, respectively. With the index, values more positive than +20 or more negative than −10 are usually considered as indicative of abnormal left and right axis deviation, respectively. The index is perhaps slightly more reliable for estimating significant left axis deviation, while the angle seems to express right axis deviation more satisfactorily. Both methods, however, are arbitrary, neither is wholly reliable, and comparison of the two indicates that they are about equally satisfactory clinically.

The reliability of axis deviation in the electrocardiogram as a method of estimating relative ventricular strain has been tested in the past: by comparing the axis deviation with (1) the relative post-mortem weights of the two ventricles, (2) the relative ventricular strain to be expected with the type of heart disease as diagnosed clinically, and (3) the relative size of each ventricle as shown by roentgenographic examination. The number of these studies is few, and the importance to be attached to them is in the order mentioned above. The difficulty of ascertaining the ratio of enlargement of the ventricles roentgenologically, except when they are very abnormal, is familiar to anyone experienced with cardiac roentgenography. On the other hand there is also difficulty in relying on current autopsy data, since ventricular volumes, as well as weights, undoubtedly should be taken into consideration.

There exist only three reports based on anatomic studies. Lewis[4] and Cotton[6] compared axis deviation and the relative ventricular weights in

15 hearts and came to the conclusion that axis deviation as estimated by electrocardiography was a reliable method of detecting ventricular preponderance, especially of the right ventricle. Later, Herrmann and Wilson,[7] as a result of similar studies on 59 hearts, questioned the validity of such a conclusion except in those cases in which considerable cardiac enlargement existed. The discrepancy in these results apparently rests upon the fact that both Lewis and Cotton used only cases in which there was marked cardiac enlargement.

The conclusions of Herrmann and Wilson are worthy of mention and have been summarized as follows:

1. The relative weight of the two ventricles is but one of many factors which influence the form of the ventricular complex of the electrocardiogram. Its influence predominates only when the heart is greatly hypertrophied. There is no definite relation between the form of the ventricular complex and the relative weight of the two ventricles when the ventricular weight is below 250 gm.

2. The chief factors which disturb the relation between the form of the electrocardiogram and the relative weight of the two ventricles, so it is suggested, are: (1) variations in the position of the heart, (2) variations in the arrangement of the ventricular conducting system, and (3) disturbances of intraventricular conduction.

3. The form of the normal electrocardiogram is not determined by the relative weight of the two ventricles; it is chiefly dependent upon the position of the heart and upon the arrangement of the ventricular conducting system; sometimes one, sometimes the other, of these factors exerts the greater influence.

Just how much importance is to be placed on differences in the architecture of the conduction system and differences in the rate of intraventricular conduction (excluding degrees which give bundle branch intraventricular block) is difficult to ascertain at present. Such concepts are still based largely on theoretical grounds.

The importance of the position of the heart with respect to axis deviation, however, is recognized clinically and has been firmly established experimentally. It is well known that the heart of the asthenic individual is usually vertically placed in the chest and that when this is the case there is a tendency for the electrical axis to deviate to the right, whereas the obese or stocky individual usually has a transverse heart with a tendency to left axis deviation. Further, it is true that roentgenographic examination of the vertical heart in the anterior position not infrequently shows slight fullness or prominence in the region of the pulmonary conus. This can be explained anatomically by slight rotation of the heart to the left around its long axis, bringing into relief the conus pulmonalis and the base of the pulmonary artery. The relationship between the position of the heart and the electrical axis has been studied experimentally both by theoretical rotation of the human

heart,[8, 9] which can be approximated by varying the position of the electrocardiographic leads, and by actual displacement experiments in animals.[10, 11] It is generally agreed that displacement to the right or left alone causes no significant alterations in the electrical axis, but that rotation of the heart, particularly about its longitudinal axis, does produce significant axis deviation. Rotation to the left about the longitudinal axis produces right axis deviation, while a reverse rotation causes the axis to deviate to the left. Meek and Wilson,[11] by correlating the anatomical studies of Groedel and Mönckeberg[12] and their own rotation experiments, bring out the significant point that the changes in the anatomical relationships of the ventricles and septum which occur when there is hypertrophy of the right or left chamber are duplicated by rotation of the heart about the longitudinal axis. There seems little doubt, then, that the position of the heart in the chest, or, perhaps better, the relative position of the ventricles and septum in the thoracic cage, is of primary importance in determining the position of the electrical axis of the heart.

Clinical studies[13, 3, 5, 14] have shown, as a rule, a correlation between the ventricular preponderance expected in a given type of heart disease and the axis deviation. Prodger and Davis[3] have shown by roentgenographic studies that the correlation between axis deviation and type of heart disease is closer in enlarged hearts than in hearts of normal size. This adds clinical support to the conclusions of Herrmann and Wilson.[7] Although there are no specific studies to substantiate the following, it seems certain that the degree and duration of the heart disease and neutralizing valvular lesions, in so far as they effect relative ventricular hypertrophy, are important factors in determining the degree of axis deviation. In this regard Thompson and White[15] have shown that in heart disease affecting primarily the left ventricle, particularly when there has been chronic left ventricular failure, there is commonly right ventricular hypertrophy which sometimes counterbalances, in part or wholly, the left axis deviation, and in a rare case is sufficient even to produce signicant right axis deviation.

DISCUSSION OF PRESENT STUDY

An analysis by ourselves of the relative frequency of right and left axis deviation in 15,000 electrocardiograms showed that significant left axis deviation was approximately five times as frequent as significant right axis deviation.* This ratio undoubtedly would favor the former even more in those regions where rheumatic heart disease is not so prevalent as in New England. In our series, for example, rheumatic heart disease accounted for almost half (45.5 per cent) of the entire number of cases of right axis deviation.

*Left axis deviation occurred 2,654 times, while right axis deviation was found in 516 cases.

TABLE I

DISTRIBUTION OF 200 UNSELECTED CASES OF RIGHT AXIS DEVIATION

CLINICAL STATUS	RIGHT AXIS DEVIATION (IN DEGREES, USING EINTHOVEN'S TRIANGLE)								
	+90° TO +94°	+95° TO +99°	+100° TO +104°	+105° TO +109°	+110° TO +114°	+115° TO +119°	+120° TO +129°	+130°+	TOTAL
Normal Hearts	15	26	21	10	2	1	0	0	75 (37.5%)
Mitral Stenosis Without Aortic Regurgitation	11	7	15	10	9	5	2	4	63 (31.5%)
Mitral Stenosis With Aortic Regurgitation	4	2	7	2	6	3	2	0	26 (13%)
Congenital Heart Disease	0	1	1	2	0	2	2	6	14 (7%)
Coronary Heart Disease	1	1	3	1	0	0	0	1	7 (3.5%)
Cor Pulmonale	2	1	0	0	0	1	0	1	5 (2.5%)
Miscellaneous*	3	4	0	2	0	0	0	1	10 (5%)
Total	36 (18%)	42 (21%)	47 (23.5%)	27 (13.5%)	17 (8.5%)	12 (6%)	6 (3%)	13 (6.5%)	200 (100%)

*Lupus erythematosus disseminatus with cardiac involvement, 2 cases; chronic constrictive pericarditis, 2 cases; acute glomerular nephritis with inverted T waves in Leads I, II, and IV, 1 case; chronic glomerular nephritis with pericarditis and inverted T waves in Leads I and IV, 1 case; thyrotoxicosis, 1 case; rheumatic heart disease with mitral regurgitation, 1 case, with slight aortic regurgitation, 1 case; and heart disease of undetermined etiology (? cor pulmonale), 1 case.

The distribution of our series of 200 cases of right axis deviation in respect to the degree of axis deviation and the clinical condition of the heart (Table I) brings out several significant points. It is interesting that almost as many patients with right axis deviation revealed no heart disease (37.5 per cent) as showed mitral stenosis (44.5 per cent). Also, it is important to note that the degree of axis deviation which occurs normally exceeds the commonly accepted upper normal limits. Furthermore, it is evident that right axis deviation of more than +109° is very rarely found normally; therefore, one is justified in considering an axis deviation of +110° or more as definite evidence of organic heart disease.

Right axis deviation without low voltage or wide QRS waves occurred in only seven cases of coronary heart disease, and even then, in only one case (autopsy) was the axis deviation of more than slight degree. In this case there was no post-mortem evidence of right ventricular strain, and the right axis deviation was in all probability due to the position of the heart. We believe that in most instances of coronary heart disease right axis deviation is to be explained on this basis. The infrequency of right axis deviation with coronary heart disease is particularly significant, since in this clinic the number of electrocardiograms taken on individuals with this type of heart disease is large. Despite the unquestionably high incidence of coronary heart disease among the 6000 individuals, there were only 7 such cases in which there was right axis deviation. One must conclude, therefore, that the finding of right axis deviation in the electrocardiogram is strong evidence that the patient does not have coronary heart disease, and, consequently, every other etiologic possibility should be excluded before such a diagnosis is made when right axis deviation is present. In our series of 200 instances of right axis deviation there were 2 cases in which coronary heart disease was diagnosed clinically, in both of which cor pulmonale was found at autopsy.

As might be expected, patients with congenital heart disease showed the greatest proportion of high degrees of right axis deviation, while those with mitral stenosis without aortic regurgitation, and with aortic regurgitation, followed in that order. One should recognize the fact that in aortic regurgitation, when there is a mid-diastolic murmur, and the question arises whether this murmur is functional (Austin Flint) or due to mitral stenosis, considerable left axis deviation favors the former, whereas no axis deviation or slight right axis deviation favors the latter.

The age distribution in these cases (Table II) is consistent with that which is to be expected from the etiology of the heart disease. The diminution in the number of subjects with normal hearts after middle age is probably to be attributed to two factors, first, the increase in the amount of coronary heart disease, either clinical or electrocardiographic, and, second, the tendency at this age for the body weight to increase,

which would cause the electrical axis of the heart to rotate toward the left, counterbalancing any pre-existing right axis deviation and in some individuals even producing some left axis deviation.

TABLE II

DISTRIBUTION OF 200 CASES OF RIGHT AXIS DEVIATION WITH RESPECT TO AGE AND CARDIAC STATUS IN INDIVIDUALS OVER 5 YEARS OF AGE

AGE	CARDIAC STATUS						TOTAL NUMBER OF CASES
	NORMAL HEARTS	RHEUMATIC HEART DISEASE	CORONARY HEART DISEASE	CONGENITAL HEART DISEASE	COR PULMONALE	MISCELLANEOUS	
5 to 9 yr.	1	3	0	1	0	0	5 (2.5%)
10 to 19 yr.	13	20	0	9	0	1	43 (21.5%)
20 to 29 yr.	30	20	0	2	0	5	57 (28.5%)
30 to 39 yr.	16	31	1	1	0	0	49 (24.5%)
40 to 49 yr.	9	12	2	1	1	0	25 (12.5%)
50 to 59 yr.	3	4	2	0	1	2	12 (6.0%)
60 to 69 yr.	2	0	1	0	2	0	5 (2.5%)
70 to 79 yr.	1	1	1	0	1	0	4 (2%)

The significant conclusions suggested by Table III may be summarized as follows: (1) the tetralogy of Fallot always causes right axis deviation,* usually of a high degree; (2) an interventricular septal defect rarely causes any deviation of the electrical axis, and, if it does, the tendency is for right axis deviation to occur; (3) patency of the ductus arteriosus almost never causes right axis deviation, but may cause significant left axis deviation; and (4) in cor pulmonale there is always right axis deviation (or a tendency to right axis deviation), although not necessarily of a high degree.

In conclusion, we wish to emphasize that axis deviation, and particularly right axis deviation, has a practical value which frequently is not appreciated. The significance of even a slight degree of right axis deviation should not be overlooked, since its proper evaluation may be of prime importance in leading to a correct clinical diagnosis. We believe that it is a wise rule to explain right axis deviation adequately in every instance. In persons with normal hearts, a vertical position of the heart in the chest or its rotation around its longitudinal axis toward the left by a thoracic or spinal deformity is the most important factor leading to right axis deviation, while in subjects with transverse or enlarged hearts, right axis deviation is almost always due to a cardiac defect which has led, either primarily or secondarily, to right ventricular strain. The effects of position and of disease may be combined in the same case.

SUMMARY

1. We have made a clinical analysis of 200 cases in which the electrocardiogram showed right axis deviation of more than +90°, excluding

*In very rare cases of the tetralogy of Fallot there is also a congenital dextrocardia which inverts Lead I and so neutralizes the right axis deviation.

TABLE III

TYPE OF HEART DISEASE		NUMBER OF CASES	LEFT AXIS DEVIATION	NO AXIS DEVIATION	RIGHT AXIS DEVIATION						RIGHT BUNDLE BRANCH BLOCK
					+90° TO +99°	+100° TO +109°	+110° TO +119°	+120° TO +129°	+130°+	LOW VOLTAGE	
Tetralogy of Fallot		15	0	0	0	1	1	2	10	0	1
Interventricular Septal Defect		14	0	11	0	1	1	0	0	0	1
Patent Ductus Arteriosus		17	4 (−7° to −40°)	11	1	1	0	0	0	0	0
Cor Pulmonale	Autopsy Cases	9	0	0	3	1	2	0	2	1	0
	Clinical Diagnosis	6	0	0	1	0	2	1	2	0	0

those with low voltage of the QRS complexes and intraventricular or bundle branch block. The most common findings were mitral stenosis, in 44.5 per cent of the cases, and no heart disease, in 37.5 per cent, leaving only 18 per cent associated with other conditions. Congenital heart disease was the third most common finding, responsible for 7 per cent of the cases.

2. The upper normal limit of right axis deviation we found to be +109°, except for 3 cases. We believe, therefore, that axis deviation of +110°, or more, practically always indicates organic heart disease.

3. Of the 200 cases of right axis deviation, coronary heart disease was found in only 7 (3.5 per cent), and in only one was it of more than slight degree. The position of the heart in the chest, rather than right ventricular strain, probably accounts for this combination. In view of the fact that the incidence of coronary heart disease is high among patients whose electrocardiograms are made in this laboratory, it is evident that the finding of right axis deviation electrocardiographically is strong, though not conclusive, evidence that the patient does not have coronary heart disease. In such cases cor pulmonale, particularly, should be considered.

4. An analysis of the electrocardiogram with regard to axis deviation in cases of cor pulmonale and of the most common types of congenital cardiac defects (tetralogy of Fallot, interventricular septal defect, and patent ductus arteriosus) led to the following conclusions: (1) the tetralogy of Fallot always causes right axis deviation, usually of a high degree, except when there is an associated congenital dextrocardia; (2) interventricular septal defect rarely causes any deviation of the electrical axis, and if it does, the tendency is for right axis deviation to occur; (3) patency of the ductus arteriosus almost never causes right axis deviation, but may cause significant left axis deviation; and (4) in cor pulmonale there is always right axis deviation (or a tendency to right axis deviation), although not necessarily of high degree.

5. We believe that even a slight degree of right axis deviation may be very significant and that its proper evaluation can be of prime importance in leading to a correct clinical diagnosis. In the normal person a vertical position of the heart in the chest or its rotation to the left around its longitudinal axis by a thoracic or spinal deformity is the most important factor leading to right axis deviation; while in the case of a transverse or enlarged heart, right axis deviation is almost always due to a cardiac defect which has led, either primarily or secondarily, to right ventricular strain.

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THE PRECORDIAL ELECTROCARDIOGRAM IN MYOCARDIAL INFARCTION

II. Observations on Cases of Infarction of the Posterior Wall of the Left Ventricle

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THE purpose of this second article of a series is to describe the potential variations of the extremities and of the precordium[1, 2] in two cases of infarction limited to the posterior portions of the left ventricle. The methods of study employed have been considered in Part I.[3] For reasons beyond our control the heart in Case 5 could not be grossly sectioned by the method devised by one of us (C. E. C.). It was otherwise examined as previously described. Standard and special electrocardiograms in Case 6 were recorded simultaneously with Lead I, and the time between the beginning of QRS in this lead and the intrinsicoid[4] deflection measured. Since these have no relation to the problem under consideration they are to be disregarded.

REPORT OF CASES

Case 5.—B. G., a 65-year-old white woman, knew that she had had hypertension for three years and diabetes mellitus for one year prior to admission. She had no cardiac symptoms until Sept. 29, 1936, when weakness and vague pains in the chest appeared. The following evening, and again on the morning of Oct. 1, she vomited about a pint of dark red blood. After the second hematemesis she was admitted to the hospital, conscious, but showing evidences of recent blood loss, namely, cold, clammy skin, ventricular and pulse rates of 120 per minute, and a blood pressure of 86/56. The rectal temperature was 98.8° F. The heart sounds were distant. Numerous premature systoles occurred paroxysmally. Abdominal examination was negative on admission. There was no evidence of congestive heart failure.

During her two weeks in the hospital nine blood examinations showed that the average number of erythrocytes was 3.0 million and that the average hemoglobin value was 10 gm. The leucocytes ranged from 13,500 to 24,250, with polymorphonuclear leucocytes varying from 83 to 93 per cent. The urine contained protein (2 plus), and occasionally a trace of sugar. The blood sugar content, determined twice, was 267 mg. per cent. The nonprotein nitrogen content of the blood was 100, 128, and 64 mg. per cent on three different occasions. At first the stools were tarry and gave a positive reaction with benzidine. Two cultures of the blood showed no growth after five days. The blood Wassermann reaction was negative. The mean blood pressure for two weeks (daily readings) was 125/68.

Therapy directed toward replacement of blood loss caused temporary improvement and a rise in blood pressure. On Oct. 5 the patient became restless and complained of discomfort under the lower portion of the sternum. For the first time, a tender, globular mass was palpated in the right upper quadrant of the abdomen. Long periods of stupor, with brief remissions, ensued. A sharp rise in

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rectal temperature, to 105° F., followed each of two direct transfusions of 300 c.c. of blood, given Oct. 6 and Oct. 8. Toward the end a bilateral suppurative parotitis developed. Rales in the bases of the lungs and pretibial edema were observed during the patient's stay in the hospital, but the edema disappeared before death, which occurred Oct. 14, 1936.

It could not be determined when occlusion of a coronary artery occurred, but from a consideration of the available facts and electrocardiograms, it appeared to have been some time between Sept. 29 and Oct. 5, 1936.

Necropsy.—The heart weighed 320 gm. The mitral and aortic valves were thickened, and the mitral annulus calcified. The wall of the left ventricle measured 15 to 17 mm. in thickness in most locations. The endocardium was smooth throughout but was discolored in an area about 3 cm. in diameter on the posterior wall of the left ventricle behind the posterior leaflet of the mitral valve. This area also included the posterior portion of the interventricular septum and extended as high as the mitral annulus. The discolored myocardium under it extended to the epicardium, and was 6 to 8 mm. thinner than other parts of the wall. Microscopic examination showed that it consisted of necrotic myocardium with young connective tissue at its margins. The remainder of the left ventricle contained microscopic areas of focal fibrosis.

The left coronary artery was patent at its origin. In the ramus descendens anterior were several eccentric plaques, some of them calcified, which reduced the lumen to less than one-third of normal at points 3 cm. and 7 cm. from its origin. The left circumflex was a small, though thin-walled, vessel. The right coronary showed eccentric intimal swellings throughout. Six cm. from its origin hyalinized intimal connective tissue made considerable encroachment on the lumen, and in the next centimeter of the vessel's extent the lumen was occluded by a fresh, organizing thrombus. Beyond the thrombus no gross or microscopic disease was found.

Electrocardiograms.—Four standard electrocardiograms were recorded between Oct. 5 and Oct. 10. The first of these showed the typical Q_3T_3 contour usually associated with recent infarction of the posterior wall of the left ventricle (Fig. 1). There were a deep Q wave in Leads II and III, low amplitude of the initial ventricular deflections in Lead II, a depressed RS-T segment in Lead I, and an elevated RS-T segment in Leads II and III. The P-R interval was 0.24 second in the first curve, and 0.16 second, or less, in subsequent ones. The last electrocardiogram taken showed less of the earlier RS-T displacement, and a considerable diminution in amplitude of all deflections. Auricular, blocked auricular, and ventricular premature systoles, and shifting of the pacemaker within the sinoauricular node were present in the earlier curves.

The extremity and precordial potentials (Fig. 1) were taken Oct. 7, 1936. In the former, the deep Q wave in Lead V_F was the only abnormality. Slight reciprocal displacement of the RS-T segment in Leads V_L and V_F was noted. The precordial potentials were recorded with the string sensitivity at seven-tenths normal (1 mv. = 0.7 cm.). There were no abnormalities of the initial ventricular deflections. The T wave in Leads V_2, V_3, and V_4 was abnormal.

CASE 6.—A 53-year-old white man was admitted to the hospital on four different occasions. The first was in November, 1933, because of the sudden onset of paresis of the extremities, loss of speech, incontinence of urine, and stupor. These symptoms disappeared after forty-eight hours. Clinical and laboratory study revealed hypertensive neuroretinopathy, proteinuria, anemia, a blood nonprotein nitrogen content of 45 to 50 mg. per cent on various occasions, and a mean blood pressure of 163/89 over a period of two weeks. The fasting blood sugar value was 215 mg. per cent, and on one occasion glycosuria was present. The Wassermann reaction on the spinal fluid was weakly positive (1 plus), and on the blood, negative.

On Dec. 25, 1933, the patient had a sudden attack of dyspnea. He was readmitted to the hospital three weeks later because of complaints referable to diminished cardiac reserve. The heart sounds were distant and a systolic murmur was heard at the apex. A teleroentgenogram showed enlargement of the heart and dilatation of the aorta. The mean blood pressure for another period of two weeks was 180/100. He was symptomatically improved after a short rest in bed.

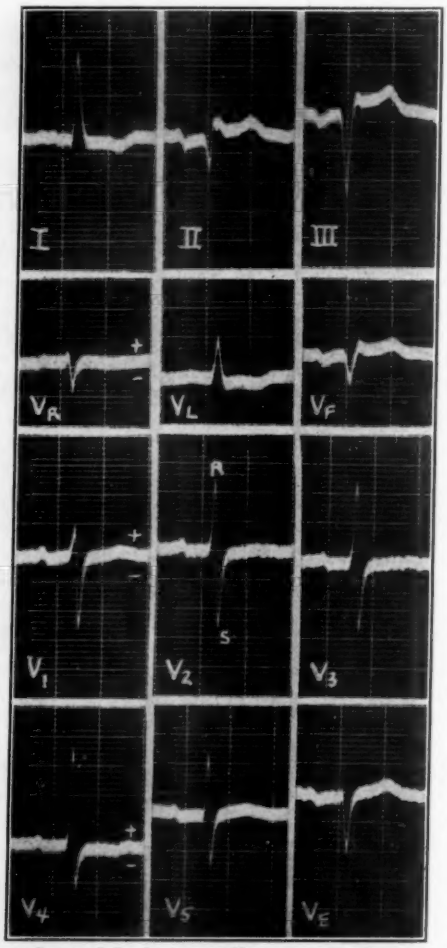

Fig. 1.—Standard and special electrocardiograms in Case 5, patient 65 years of age. The exact time of the coronary occlusion could not be ascertained but was definitely less than one week before the curves were taken. In the special electrocardiograms an upward deflection represents positivity of the exploring electrode. The sensitivity of the string for the standard leads and for the extremity potentials is normal, for the precordial potentials seven-tenths normal (1 mv. = 0.7 cm.). Time lines occur every 0.2 second.

The patient was seen briefly in May, 1934, for progressive blindness in the left eye due to cataract and retinitis. He was not heard from again until congestive heart failure and uremia appeared in March, 1935. The latter was presumably precipitated by an ascending infection of the genitourinary tract, and by retention of urine due to a urethral stricture. Death occurred in coma on April 8, 1935. The nonprotein nitrogen content of the blood was 90 mg. per cent.

The time when myocardial infarction occurred was uncertain, but it was possibly in December, 1933.

Necropsy.—The heart weighed 600 gm. The thickness of the wall of the right ventricle varied from 5 to 8 mm.; of that of the left ventricle from 16 to 22 mm.; and of the interventricular septum from 20 to 25 mm. No evidence of infarction was found until the transverse sections were made. Small areas of fibrosis were

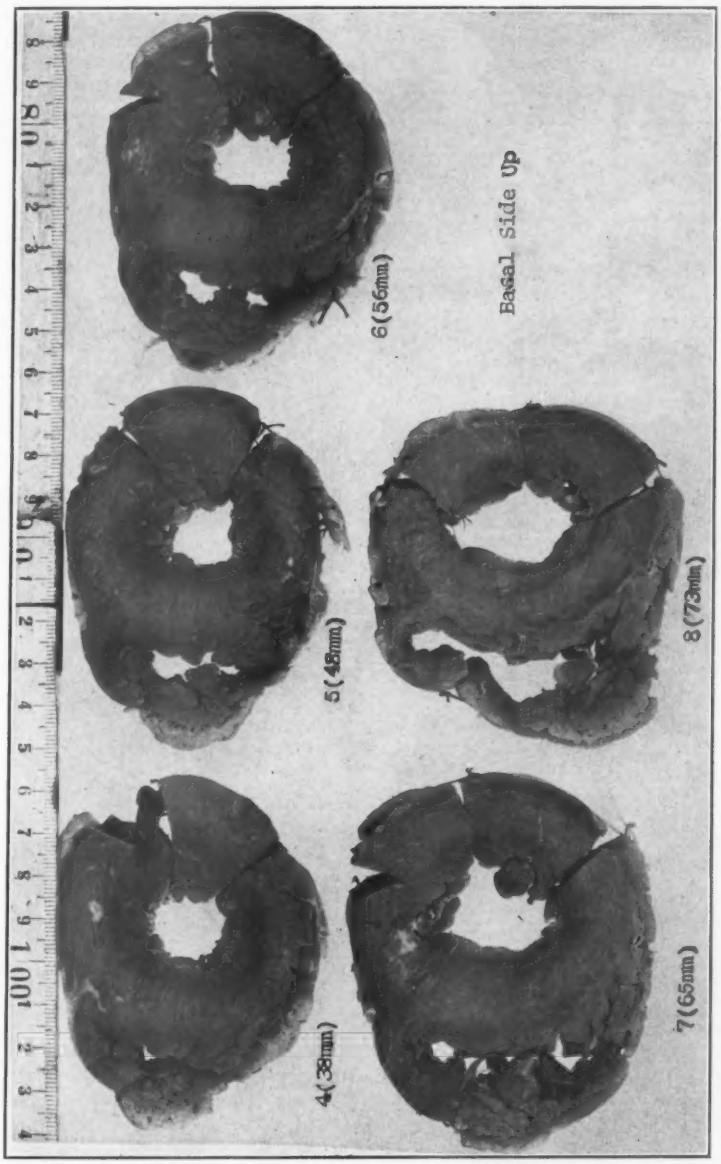

Fig. 2.—Heart sections in Case 6. The basal surfaces are visible, and the anterior wall is below. The infarct is the white area visible in the posterior wall of sections 6 and 7 (arrows). Smaller scars can be seen in the posterior wall of section 4, and in the anterior wall of section 5. The small, dark swelling on the lateral wall of the right ventricle of section 6 is a pericardial cyst.

visible grossly in various parts of the left ventricle. The largest was in the posterior wall at levels of 56 mm. and 65 mm. from the apex, respectively (Fig. 2, sections 6 and 7). It was roughly fusiform in shape, with a length of 15 mm. and a diameter of 5 mm. in its widest part. Its long axis was parallel to the long axis of the heart. Microscopically it consisted of avascular and acellular fibrous tissue.

The morbid anatomy of the coronary arteries was as indicated in Fig. 3. The artery of supply to the scar in the posterior wall of the left ventricle described above was the ramus marginis obtusi. It was occluded by atherosclerosis at its origin from the left ramus circumflexus. Moderate atherosclerosis was present in all of the major coronary branches, as indicated in the figure. The ramus descendens posterior arose anomalously from the left coronary artery.

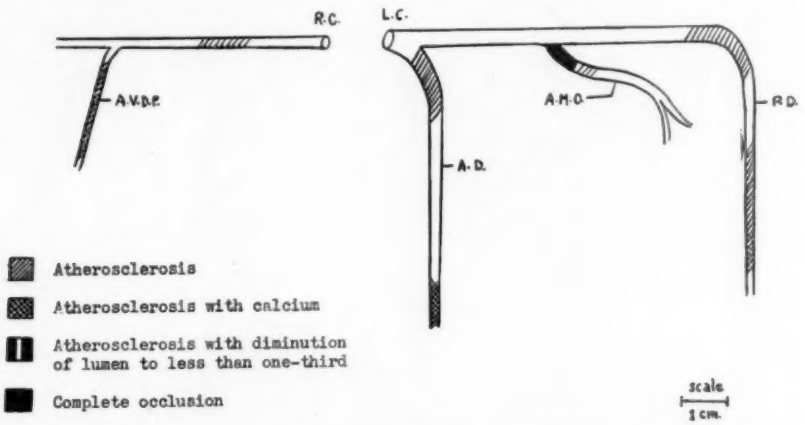

Fig. 3.—Diagram of coronary arteries in Case 6. The ramus descendens posterior arises anomalously from the left coronary artery. *L. C.*, left coronary artery; *A. D.*, ramus descendens anterior; *A. M. O.*, ramus marginis obtusi; *P. D.*, ramus decendens posterior; *R. C.*, right coronary artery; *A. V. D. P.*, ramus ventriculus dexter posterior.

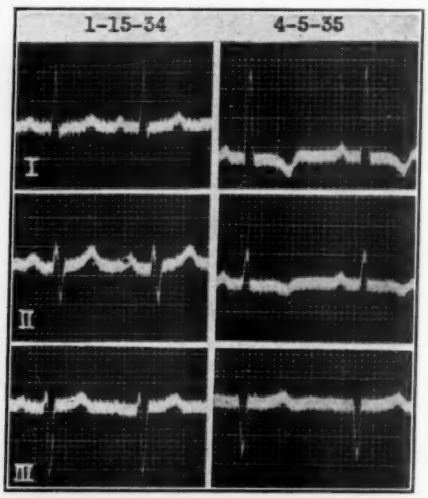

Fig. 4.—Standard electrocardiograms in Case 6, taken approximately fifteen months apart. The string sensitivity is normal. Time lines occur every 0.04 sec.

Electrocardiograms.—Standard electrocardiograms were recorded Jan. 15, 1934, and April 5 and 6, 1935 (Figs. 4 and 5). The first showed a marked sinus arrhythmia and shifting of the pacemaker within the sinus node; the others showed a normal sinus rhythm. The difference between the initial ventricular deflections in the first curve (Fig. 4) and the last two (Figs. 4 and 5) is in part attributable to the fact that the former was taken with the patient seated, the latter while he was

supine. In the second and third electrocardiograms, however, the inverted T wave in Leads I and II could not be ascribed to change in posture alone (Figs. 4 and 5).

Precordial and extremity potentials (Fig. 5) were recorded on April 6, 1935, after the patient had received twelve cat units of digitalis by mouth. This amount had no

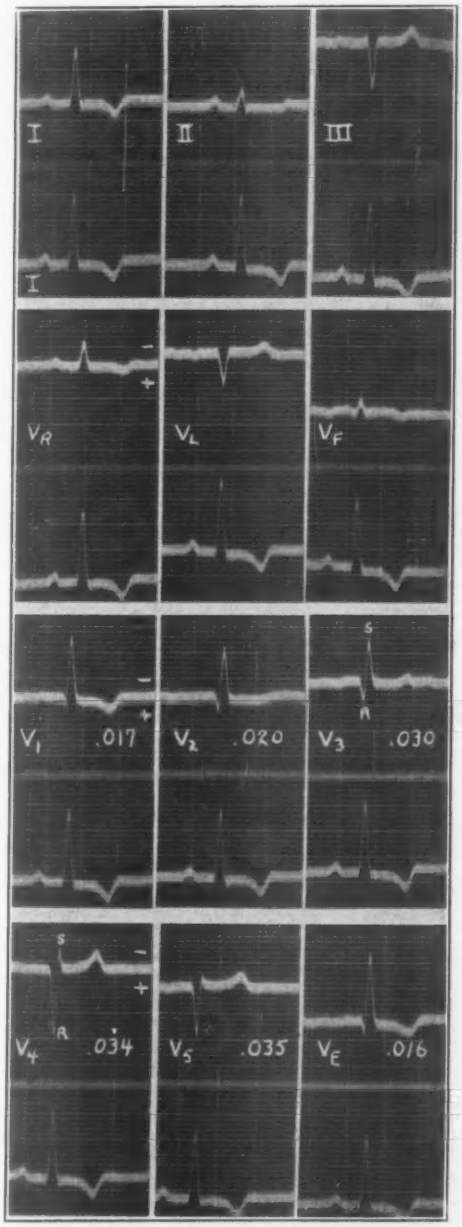

Fig. 5.—Standard leads, extremity potentials, and precordial potentials in Case 6, patient 50 years of age, recorded April 6, 1935, simultaneously with Lead I (lower curve in each illustration). Death occurred two days later. The string sensitivity is half normal for the chest leads, normal for the others. The figure under each precordial lead represents the time in seconds between the peak of R of the chest lead and the beginning of QRS in Lead I. An upward deflection of the string represents negativity of the exploring electrode.

effect on the T wave of the standard leads, and probably little, if any, on the T wave of the special leads. The initial ventricular deflections were not abnormal in the chest leads. The T wave in Leads V_R, V_2, V_3, V_4, and V_5 was abnormal.

DISCUSSION

In accordance with the laws governing electrical currents in volume conductors,[5-8] an electrode on the chest will be influenced most by those muscle elements closest to it. The truth of this is borne out by the change in contour of the ventricular complex as an exploring electrode is placed on various parts of the exposed animal[2, 9, 10] or human[11] heart, or on various parts of the animal[9, 10] or human[10, 12, 13] precordium. The initial positive deflection, or R wave, of the precordial electrocardiogram is ascribed to the passage of an action current from the endocardium to the epicardium of the muscle near the exploring electrode.[14] It would be expected, therefore, that electrically inactive muscle in the posterior or diaphragmatic regions of the heart would have little effect on the initial ventricular deflections of the precordial electrocardiogram, provided that the muscle of the anterior wall were normal. Cases 5 and 6 are examples. Others have been reported which substantiate these considerations.[15, 16]

The origin of the deep Q wave in Leads II and III in Case 5 is partly brought to light by a consideration of the extremity potentials (Fig. 1). In a series of thirty normal subjects,[12] the largest Q wave encountered in Lead V_F was 0.12 mv. In Case 5 it was 0.40 mv. Although the infarct was described as being in the posterior wall of the heart, actually, with the heart in the body, it must have been close to, or even resting on, the diaphragm, making its relation to the left leg such that, in effect, this extremity was a semidirect lead from the cavity of the left ventricle.[9] It was, therefore, negative for the greater part of the QRS interval. Since Lead II is Lead V_F minus Lead V_R, and Lead III is Lead V_F minus Lead V_L, the reason for the deep Q wave in the standard leads becomes clear when the extremity potentials are examined (Fig. 1). This wave is smaller in Lead II than in Lead III because the potential of the right arm is, in the main, negative during the QRS interval, a fact attributed to the circumstance that the right arm is attached to the trunk opposite the auriculoventricular orifices at the base of the heart.[12] If the peak of S in Lead V_R were simultaneous with the peak of Q in Lead V_F, the flow of current through the string would be slight or absent, and it is likely that no Q wave would be found in Lead II. In this instance, however, the peak of S occurred somewhat later and was approximately simultaneous with, and therefore responsible for, the first apex of the R wave in Lead II. Thus, the Q wave in Lead II depends almost entirely upon the negative variation in potential of the left leg. In Lead III, on the other hand, it is almost equally dependent upon the

negative potential of the left leg and the simultaneously positive potential of the left arm.

Abnormalities of the final ventricular deflections (RS-T) of the chest leads in Case 5 are more difficult to explain than the absence of the abnormalities in the initial ventricular deflections. Changes in these waves are sometimes extreme in cases of infarction of the posterior wall;[17] in others they are absent. The reasons for these differences in the electrocardiograms of patients with similar myocardial lesions are at present unexplained.

The cause of the T-wave abnormalities, both in the standard and special leads in Case 6, is not clear. It is probable that ventricular hypertrophy, coronary insufficiency, azotemia, and unknown factors played some part. Considering the nature of the myocardial disease and the inverted T wave in Lead I, it is unlikely that the infarct in the posterior wall was in any way related to the abnormalities noted in the final ventricular deflections. The curves emphasize the fact that T-wave changes may be marked without recent infarction to account for them. These deflections in the chest leads in Case 6 are to be compared with the same leads in Case 4 of Part I.[3] The difference between the two is that the T wave in the former is strikingly negative only in those precordial leads (V_4 and V_5) with a large R wave. It will be recalled that the heart in Case 4 showed an infarct in the anterior interventricular septum.

SUMMARY

The potential variations of the extremities and of six precordial points were correlated with the pathologic changes in the hearts in two cases. In the first, a recent infarct extended through the basal portion of the posterior wall of the left ventricle and involved the adjacent interventricular septum. In the second, a small, healed infarct, surrounded by healthy muscle fibers, was present in the basal half of the posterior wall of the left ventricle.

Infarction of the extent found had no appreciable effect on the initial ventricular deflections of the precordial electrocardiograms. In the first case the potential of the left leg (Lead V_F) was, in the main, negative during the inscription of the initial ventricular deflections, presumably because the dead muscle was so oriented that the left leg was a semidirect lead from the involved area. It is pointed out that this circumstance was the one responsible for the deep Q wave in Lead II, and in part for the deep Q wave in Lead III.

The T-wave abnormalities could be attributed in the case of recent infarction (Case 5) to no anatomic cause other than the infarct itself. In the second case, the T-wave abnormalities were probably not related to the infarcted muscle.

(References at End of Part III)

THE PRECORDIAL ELECTROCARDIOGRAM IN MYOCARDIAL INFARCTION

III. Observations on Cases in Which the Lesions Were Diffuse

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ABNORMALITIES that may be observed in the precordial electrocardiogram when there is infarction of the anterior or posterior portions of the heart have been considered previously.[3, 18] The present article deals with the potential variations of the extremities and of the precordium in three cases in which the cardiac changes were diffuse. The methods were the same as those used in the previous studies.[3, 18]

REPORT OF CASES

Case 7.—M. D., a 45-year-old white woman, had polyarthritis at the age of 23 which incapacitated her for six weeks. Thereafter mild joint pains recurred for three or four years. At the age of 43 she was told she had hypertension. It was not until she was 45 that she had cardiac symptoms. The first of these were substernal pain and dyspnea on effort in August, 1934. Progression in the severity of these symptoms made her seek the advice of a physician about the middle of October, 1934. Digitalis and rest in bed caused no improvement.

At 1 A.M. on Oct. 25, the patient had a severe anginal attack accompanied by nausea, vomiting, and collapse. Soon afterward she was admitted to the hospital with pulmonary edema and in shock. The heart sounds were inaudible. The pulse rate was 116 per minute. The blood pressure was 98/70.

The patient partially recovered within the next few hours. During the eighteen days in the hospital, however, attacks of substernal and precordial pain, usually accompanied by dyspnea, cyanosis, nausea, retching, cold sweat, apprehension, rapid pulse rate, and fall in blood pressure occurred almost daily. These would continue for about thirty minutes. When the heart sounds were audible, they were of poor quality. A systolic murmur, a precordial friction rub, and gallop rhythm were noted at one time or another at the cardiac apex.

The mean blood pressure while the patient was in the hospital (seventeen daily readings) was 108/74. The rectal temperature did not exceed 100.6° F. at any time. A blood Wassermann reaction was strongly positive (4 plus).

The patient died during one of the anginal episodes on Nov. 11, 1934, three months after the onset of cardiac symptoms.

Necropsy.—The heart weighed 340 gm. There were several small, opaque, fibrous epicardial patches. The mitral leaflets were vascularized, somewhat thickened by fibrous tissue, and partially fused at the commissures. The myocardium was soft and flabby. In the transverse sections a large scar could be seen extending from epicardium to endocardium in the posterior wall of the left ventricle, near the apex. Toward the base, minute scars were visible in various parts of the left ventricle. In the anterior wall of this chamber, and in the anterior portion of the interventricular septum of the apical sections, the subendocardial myocardium was mottled by

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dark red, irregular patches. Three centimeters above the apex this mottling involved the inner half of the entire left ventricular wall and the left side of the anterior one-third of the interventricular septum (Fig. 1). Microscopically, the dark areas consisted of focal hemorrhagic necrosis with early replacement fibrosis which was discernible especially in the posterior wall. The myocardium of the anterior and lateral walls of the right ventricle was extensively infiltrated with fat.

Occlusive disease of the coronary arteries was limited to the ostium and first centimeter of the left main stem. The margins of the ostium were elevated by intimal atheroma. The point of a cartilaginous spicule, 4 mm. in length, protruded from the orifice. The spicule was attached to the walls of the left coronary artery about 3 mm. from the ostium, and almost completely occluded its lumen. In the remainder of its extent the lumen of the artery was greatly reduced in size by intimal thickening. Microscopically, the lesion consisted of irregular intimal and adventitial fibrosis. Some of the vasa vasorum in the aorta adjacent to the mouth of the left coronary showed hypertrophy of the media. There was no evidence of syphilitic mesaortitis. The ramus descendens and the ramus circumflexus of the left coronary artery were free from disease. Slight focal intimal thickening was present in the right coronary artery near its origin.

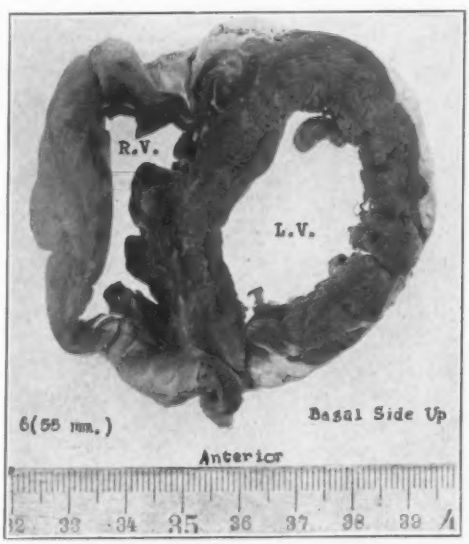

Fig. 1.—Heart section 6, Case 7, basal side up. The dark patches in the subendocardium are areas of hemorrhagic necrosis (arrows). Fine scarring is visible in the septum. The lateral wall of the right ventricle is infiltrated with fat.

Electrocardiograms.—Eight standard electrocardiograms were taken between Oct. 25 and Nov. 7, 1934. All showed sinus rhythm with occasional ventricular premature systoles, and a P-R interval between 0.23 and 0.25 second. The rate of the auricles and of the ventricles ranged between 100 and 120 per minute. In all curves the mean electrical axis was deviated to the left and made an angle with the horizontal (angle alpha) of approximately -38°. The initial and final ventricular deflections were much as they are in the standard leads of Fig. 2, except that in the later curves RS-T displacement was less pronounced. The S wave was prominent in Leads II and III, but no Q wave was present in Lead I.

Potential variations of the extremities and of the precordium were recorded Oct. 25 and 27, 1934. The two sets of curves were almost identical. Those taken

on the latter date are shown in Fig. 2. The potential of the left arm was positive, for the most part, during the inscription of the initial ventricular deflections. The RS-T segment showed slight positive displacement in Lead V_R, and slight negative displacement in Lead V_F. In Leads V_1, V_2, V_3, and V_E the only initial deflection was a Q wave. The first limb of this deflection was prominently notched in Lead V_3. The R wave in Lead V_4 and the RS (intrinsicoid) deflection in Lead V_4 and Lead V_5 were abnormally small. The T wave was almost isoelectric in all of the precordial leads.

CASE 8.—G. C., a 52-year-old white man, had an attack of "acute indigestion," characterized by low substernal and epigastric pain, accompanied by dyspnea, in 1928, as a result of which he was in a hospital for five days. Thereafter, he remained well until paroxysms of dyspnea and substernal pain appeared in 1934. These symptoms gradually increased in frequency and severity. At 10 P.M. on Jan. 16, 1935, a severe attack of pain and dyspnea occurred which lasted for five hours. He was admitted to the hospital Jan. 17, soon after its onset. He was dyspneic, orthopneic, and cyanotic. Rales were present in both pulmonary bases, and there was slight pretibial edema. The heart was greatly enlarged. At the apex the first sound was snapping. The ventricular and pulse rates were 96 per minute; the beating was regular. The blood pressure was 165/92 and stayed approximately at this level for the remainder of the patient's life. Two blood Wassermann reactions were moderately (2 plus) and doubtfully (plus-minus) positive, respectively.

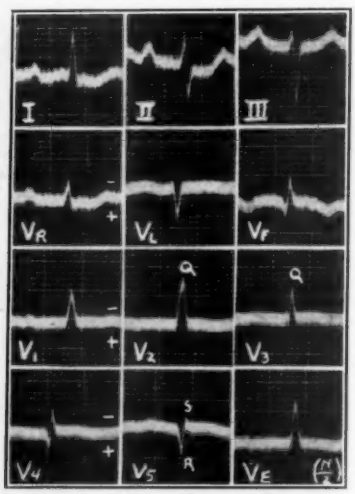

Fig. 2.—Standard and special electrocardiograms in Case 7, patient 45 years of age, recorded Oct. 27, 1934, two weeks before death. An unknown amount of digitalis had been taken by mouth. Standard leads and extremity potentials were recorded with the string at normal sensitivity; precordial potentials were recorded at half-normal sensitivity. An upward deflection represents relative negativity of the exploring electrode. Time lines occur every 0.2 second. The electrocardiograms reproduced in Figs. 6 and 7 were similarly recorded.

The patient improved with rest in bed but continued to have dyspnea which was worse at night. On Jan. 26 he had a slight rise in temperature and complained of a sore throat. The pharynx and tonsils were inflamed. A hemolytic streptococcus grew in the culture of the throat swabbings. Three days later, at 8 P.M., the patient had a severe paroxysm of dyspnea. On Jan. 30 digitalis was started, but no improvement occurred. He died suddenly on Feb. 8, 1935.

Necropsy.—The heart weighed 610 gm. The visceral and parietal pericardium were firmly adherent over the bulging apex and adjacent anterior wall of the left ventricle (Fig. 3). The endocardium of the left ventricular apex, the anterior interventricular septum, and the anterior wall was pale, thick, and opaque. The endocardium of the posterior wall of this chamber and of the nearby septum was dark red in color, and the underlying muscle felt softer than elsewhere. The right ventricle was hypertrophied; its wall measured 1.5 cm. in thickness in its posterior basal portion.

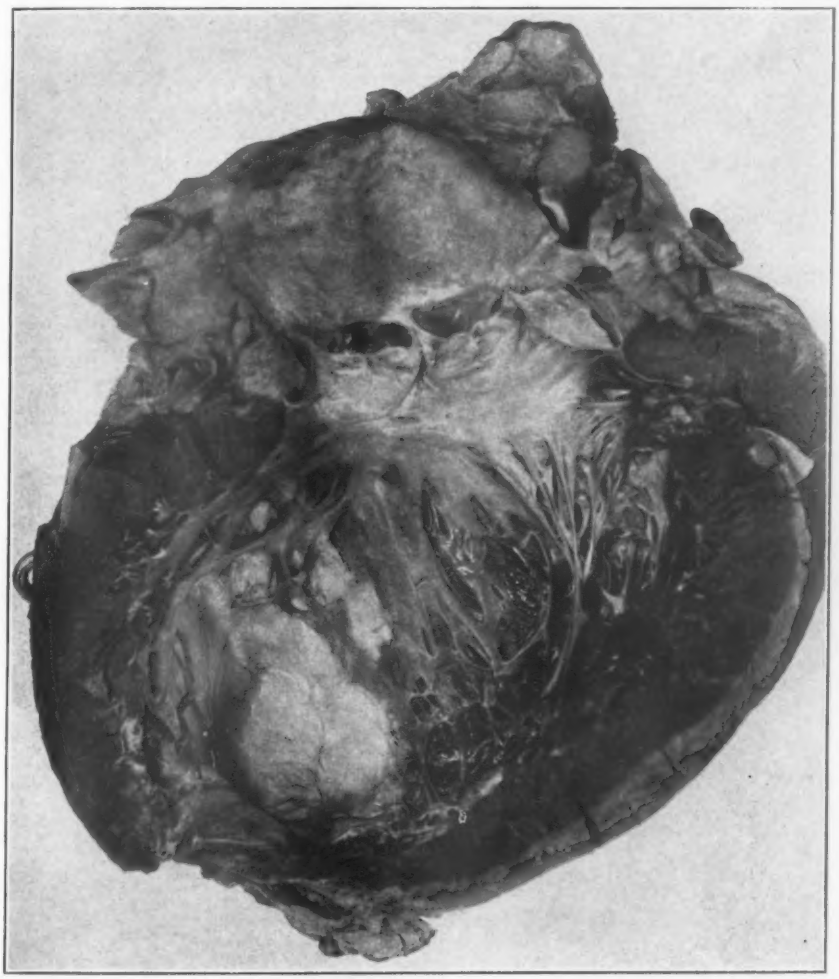

Fig. 3.—Heart in Case 8, viewed from the left. The anterior wall is to the left. The thin, bulging apex, the thick endocardium of apex and septum, and the adherent pericardium (below) are to be noted.

The transverse sections (apical surfaces seen in Fig. 4) showed the diffuse lesions to greater advantage. All that remained of the anterior and lateral portions of the left ventricular apex was a thin layer of muscle, bounded by thick, acellular and avascular endocardium and fibrotic pericardium (Fig. 4, sections 2, 3, and 4). Between the pericardium and the rim of muscle there was a thick layer of fibrolipomatous tissue. This tissue (labeled *A* in sections 3 to 6) was most ex-

tensive in the anterior interventricular sulcus and along the adjacent anterior wall of both ventricles. At the base the layer of myocardium was thicker, and the lesion was limited to the anterior wall of the left ventricle and the nearby thinned septum. Extending from a point about 25 mm. from the apex to the

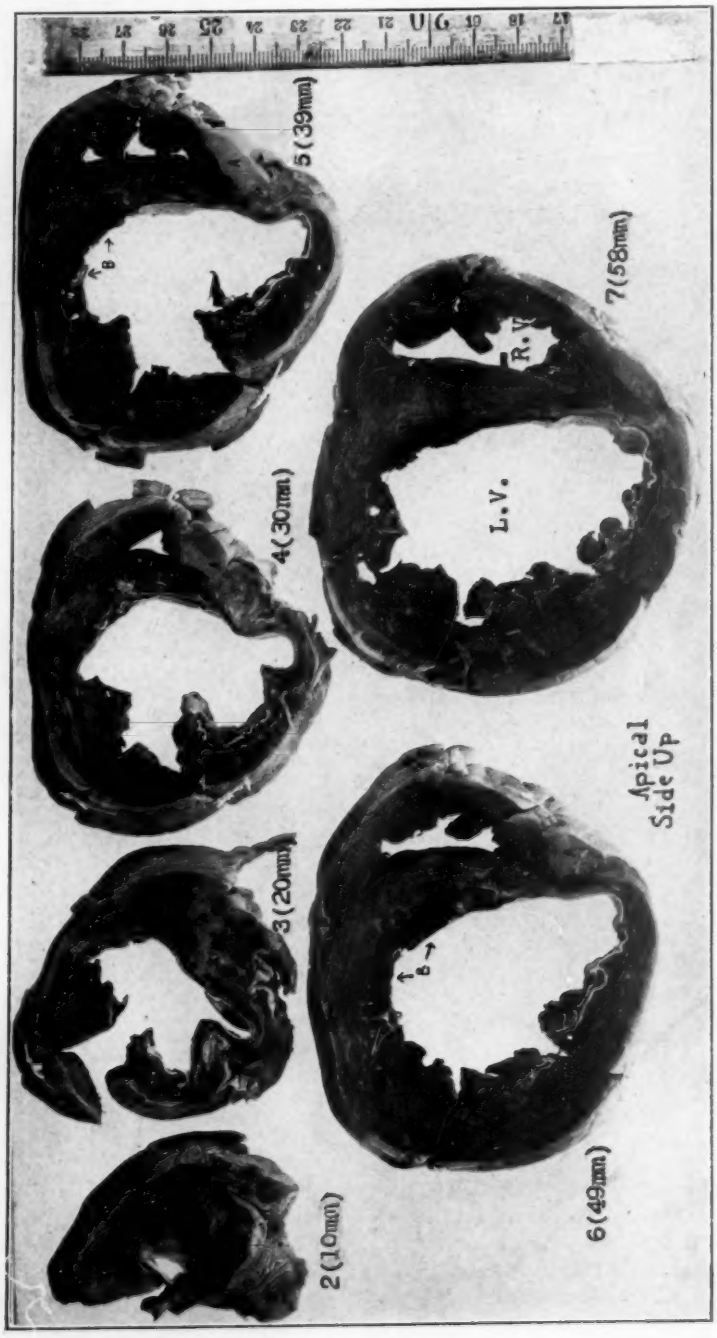

Fig. 4.—Heart sections in Case 8. Contrary to the usual procedure, the apical surfaces of the sections were photographed. The left ventricle is to the left and the anterior wall below. The thick endocardium is white. The increased subepicardial fat *A* is especially prominent in the anterior interventricular groove of sections 4 and 5. The dark areas in the posterior wall *B* of the basal sections represent hemorrhage into scar tissue. The pericardium is adherent to the apical sections (*2* and *3*).

basal extremity of the posterior wall, there was a lesion of somewhat different nature (labeled *B* in sections 5 and 6). Grossly, it had a dark red, patchy appearance. It was confined largely to the inner half of the wall and extended somewhat into the left side of the posterior part of the septum. Microscopically, it consisted of scar tissue containing large blood-filled sinusoids and extensive areas of hemorrhage. Near the apex, fresh granulation tissue was seen in the posterior wall, replacing a small area of necrotic muscle cells.

The coronary arteries were extensively diseased (Fig. 5). The first two centimeters of the ramus descendens anterior contained a hyalinized, calcified plaque which decreased the lumen to about one-tenth of its original size. Beyond this obstruction the wall was thick and calcified. The first portions of the ramus circumflexus and of the ramus marginis obtusi were atherosclerotic. The right coronary artery was stenosed at points 0.5 cm. and 5.5 cm. from its origin. Elsewhere there were patchy sclerosis and calcification. Its ramus descendens posterior was calcified in its entire extent, but a sizeable lumen remained.

Electrocardiograms.—Four standard electrocardiograms were taken between Jan. 18 and Feb. 6, 1935. All showed sinus rhythm and a rate between 85 and 110 per minute; a QRS interval of 0.08 to 0.09 second; and a considerable deviation of the electrical axis to the left (angle alpha of approximately -40°). The initial ventricular deflections were similar in all. The Q wave in Lead I and the R wave in Leads II and III were minute deflections, and in some curves an R wave could not be distinguished in Lead II. The S wave in Lead II was slurred, in Lead III, deep. The T wave was inverted in Lead I, isoelectric in Lead II, and upright in Lead III. Only minor differences in this deflection could be discerned in successive electrocardiograms before the administration of digitalis was started.

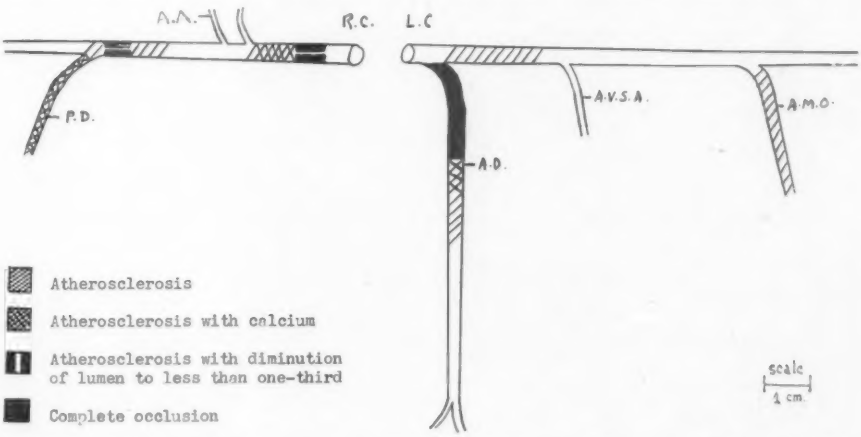

Fig. 5.—Diagram of coronary arteries in Case 8. *L. C.*, left coronary artery; *A. D.*, ramus descendens anterior; *A. V. S. A.*, ramus ventriculus sinister anterior; *A. M. O.*, ramus marginis obtusi; *R. C.*, right coronary artery; *A. A.*, rami auricularis; *P. D.*, ramus descendens posterior.

Extremity and precordial potentials were recorded Jan. 21, 1935 (Fig. 6). Abnormalities in the former were the small T wave in Lead V_R, the large R wave in Lead V_L, and the deep Q wave in Lead V_F. Abnormalities in the initial ventricular deflections of the latter were the small R wave in Leads V_2 and V_3, the four QRS deflections in Lead V_4, and the deep S wave in Lead V_E. Of the final ventricular deflections, the diphasic T wave and the negative T wave in Leads V_4 and V_5, respectively, were abnormal. Of interest was the QRS interval in Lead V_5, which measured 0.108 second, compared to that in Lead II, which measured 0.088 second.

CASE 9.—F. C., a 62-year-old white man, was admitted to the hospital May 18, 1936, with congestive heart failure. His mental state was such that a reliable history could not be obtained. He indicated, however, that he had substernal pain.

The heart was enlarged; the sounds were of poor quality. A systolic murmur was heard at the apex, another at the base. The ventricular and pulse rates were 80 per minute. The beating was regular. The blood pressure was 130/50 and averaged 137/63 during the next two weeks. Respiration was of the Cheyne-Stokes type.

Lethargy and dyspnea were prominent symptoms. Digitalis, begun on May 18, was without effect. Splenic enlargement and conjunctival petechiae were noted a few days after admission. A low-grade fever was present. Blood cultures were positive for the *Streptococcus viridans* on three different occasions. Wassermann reactions on the blood and spinal fluid were negative.

Somnolence rapidly deepened to stupor. The patient died May 31, 1936.

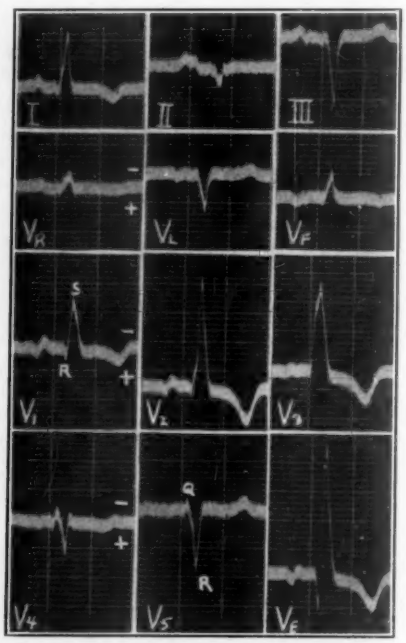

Fig. 6.—Standard leads (I, II, III), extremity potentials (V_R, V_L, V_F), and precordial potentials (V_1, V_2, V_3, V_4, V_5, V_6) in Case 8, patient 52 years of age, recorded Jan. 21, 1935, eighteen days before death.

Necropsy.—The heart weighed 500 gm. There was slight sclerosis of the mitral, aortic, and tricuspid valves. Vegetative endocarditis (*Streptococcus viridans*) involved the mitral and aortic leaflets, the chordae tendineae of the anterior mitral leaflet, an area, 2 cm. by 2 cm., of the left auricle just above the posterior mitral leaflet, and a small patch, 0.6 cm. by 1.0 cm., on the left side of the interventricular septum, 0.5 cm. below the aortic valve.

Grossly, the myocardium showed little. The lateral wall of the left ventricle measured 18 to 20 mm. in thickness; that of the right ventricle, 5 to 7 mm. The transverse sections showed slight subendocardial discoloration in the left ventricle, focal endocardial thickening, and focal myocardial fibrosis. On microscopic section, however, there were miliary foci of necrosis, some undergoing replacement fibrosis,

disseminated throughout both ventricles and auricles. These were especially prominent and tended to be confluent in the subendocardial myocardium of the left ventricle. In addition, there were older, loose perivascular and interstitial fibrosis, atrophic muscle cells, and occasional foci of subacute productive myocarditis. The pericardium was focally thickened over both ventricles. The thickened areas were infiltrated by lymphocytes and histiocytes.

The coronary ostia were widely patent. The intima of the ramus descendens anterior was thickened by eccentric hyalinized plaques which, at a distance of 2 cm. from the vessel's origin, reduced its lumen to a diameter of 1 mm. This severe stenosis extended distally for 0.5 cm. The left ramus circumflexus and the right coronary artery showed intimal atheroma in the first few centimeters, but neither of their lumina was appreciably reduced in size.

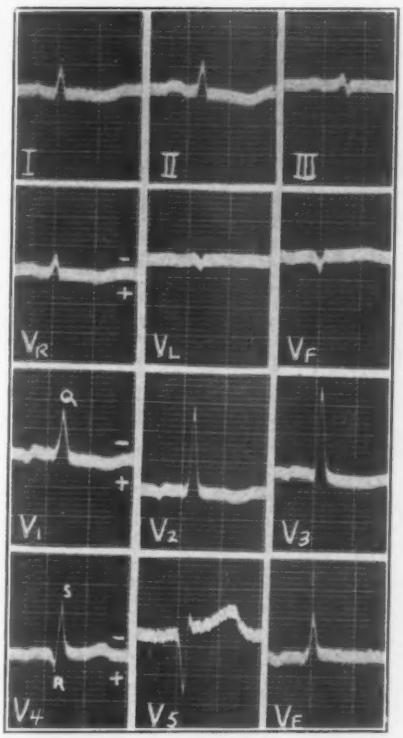

Fig. 7.—Standard and special electrocardiograms in Case 9, patient 62 years of age, recorded eight days before death. A therapeutic dose of digitalis had been administered in the preceding five days.

Electrocardiograms.—Six standard curves were recorded between May 18 and 28, 1936. Only the first of these was obtained before the administration of digitalis was started. The heartbeat had its origin in the sinoauricular node and was regular in all. The rates varied between 90 and 100 per minute. The P-R and QRS intervals were within normal limits. The amplitude of the initial ventricular deflections was low (Fig. 7). In the first electrocardiogram the T wave was low in Lead I, isoelectric in Lead II, and small, but inverted, in Lead III. In all subsequent curves this deflection was inverted in the three leads, though small in Lead III (Fig. 7).

The extremity and precordial potentials (Fig. 7) were recorded May 23, five days after the administration of digitalis was begun, and eight days before the pa-

tient died. A deep Q wave in Leads V_1 and V_E, a small R wave in Leads V_2, V_3, and V_4, and a negative T wave in Leads V_4 and V_5 were the significant abnormalities in the precordial leads. The extremity potentials were small, and the positive T wave in Lead V_R was abnormal. In the special leads little significance could be attached to the abnormal final ventricular deflections because the patient was digitalized.

DISCUSSION

The QRS complexes in the chest leads in Cases 7 (Fig. 2) and 9 (Fig. 7) were rather similar in form. The chief difference between the two was the small R wave in Leads V_2 and V_3 of the latter. In Lead V_3, in Case 7 (Fig. 2), the R wave was presumably represented by the notch on the first limb of the Q wave.

The resemblance of the disease of the myocardium in these two cases was also striking. In both there was myocardial necrosis which was diffuse but principally located in the subendocardium of the anterior part of the left ventricle. In Case 9 there were, in addition, scattered foci of subacute productive myocarditis. From what was said about the R wave in Part I,[3] it seems plausible to assume that the small size or absence of this deflection in several of the leads in the cases under discussion was due to this necrosis.

The changes in QRS of the precordial electrocardiograms were principally in leads from the right side and midportion of the chest. In both of the cases there were lesions in the right ventricle. In one it was extensive fatty infiltration; in the other it was focal myocardial necrosis. It cannot be stated that this disease in the right ventricle had any effect on the chest leads, because, as previously noted,[3] the R wave may be absent or diminished in size in leads from the right side of the precordium when disease of the myocardium is limited to the left ventricle and septum. That more marked abnormalities of QRS were not found in leads from the left side of the precordium is probably due to the fact that the lesions were principally in the anterior part of the heart.

Case 8 is unusual in several respects. Considering the extent of the lesion found at necropsy, it is somewhat of a surprise that more marked abnormalities were not present in the extremity and precordial potentials. In Lead V_F the only QRS deflection was a Q wave, 0.35 mv. in size. In the only other case of the series in which this abnormality existed there was a fresh infarct on the posterior wall of the left ventricle (Case 5, reference 8). In Case 8 the lesion on the posterior wall was a scar into which hemorrhage had recently occurred. It would seem that a Q wave in Lead V_F is of some value in localizing electrically inactive muscle in the posterior (diaphragmatic) wall of the heart.

In the chest leads in Case 8 the small R wave was again the most notable feature. The low, though broad, negative deflection in Lead

V_4, which ordinarily would be designated as Q, was in this instance preceded by a minute positive deflection, an explanation for which is lacking.

The QRS interval of 0.106 sec. in Lead V_3, compared to an interval of 0.088 in Lead III, is of interest. Such a discrepancy must occur more frequently than is suspected, for the standard leads represent the difference in potential between two extremities, and if the potential of these extremities varies in a similar manner either at the beginning or end of the initial ventricular deflections, no current will flow through the string, and the QRS interval will be correspondingly shortened. Further, the standard leads record electrical forces in the frontal plane, or those making a relatively acute angle with this plane. Currents generated in the anteroposterior plane affect all three extremities similarly. Therefore, they cause no deflection in the standard leads but may cause a sizeable one in the chest leads. This would, conceivably, account for variations in the QRS interval in the two types of leads. Differences in the duration of QRS in different chest leads are due, at least in part, to this same factor.

The factors responsible for abnormalities of the T wave in the cases just discussed are so numerous that more than mention of them does not seem justified at this time.

SUMMARY

The potential variations of the extremities and of six precordial points were correlated with the diffuse lesions found in the hearts in three cases. In two of these the changes were similar. In one they consisted of disseminated miliary necrosis and foci of subacute productive myocarditis in both ventricles; in the other there were acute, healing, and healed focal necrosis of the left ventricle and septum, and fatty infiltration of the right ventricle. The QRS complexes of the special electrocardiograms were similar to each other in these two cases and simulated those seen with various degrees of infarction of the anterior wall of the left ventricle. In the remaining case the infarct consisted of old fibrous tissue, located anteriorly and posteriorly. The posterior portion was electrocardiographically reflected in the extremity leads by a deep Q wave in Lead V_F. The anterior portion was held responsible for the low R wave in leads from the right side and midportion of the precordium, and for a prominent early negative deflection in Lead V_4.

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METHOD FOR THE STUDY OF VENTRICULAR FIBRILLATION

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INVESTIGATORS have hitherto relied mainly on electric shock to produce experimental ventricular fibrillation.[1, 2, 3, 4] For quantitative studies the intensity of electrical stimulation necessary to produce ventricular fibrillation under varying conditions has been determined, and electrocardiograms have been obtained either by limb leads, or directly from the exposed heart. Extensive studies[2, 4] have been made of the effect of drugs on electrically produced fibrillation.

With these methods, however, many complicating factors are involved, since the heart may also be affected indirectly by changes produced in other parts of the body. The aim of the present study was to confine the action to the heart alone, so as to be able to determine a "fibrillation level" for the myocardium under standard, controlled conditions. For this purpose the isolated, perfused heart was used, and ventricular fibrillation was produced by the action of barium chloride.

METHOD

The heart of the cat, dog, or rabbit was isolated immediately after death by bleeding and was perfused through the coronary system with oxygenated Locke's solution by a modification of the Langendorff method. The temperature of the heart and perfusing fluid was kept constant at 38° C. by means of a water bath and warm chamber controlled by a thermostat, and the perfusion pressure was maintained at 80 mm. Hg for the rabbit heart, and 100 mm. Hg for the cat or dog heart. Slight changes of the perfusion pressure did not appear to affect the results. Perfusion was continued usually for ten or fifteen minutes, until the heart was beating steadily, and the coronary flow, measured approximately by collecting the outgoing fluid, was constant. Then, without alteration of pressure or temperature, the perfusate was changed to Locke's solution containing 0.2 per cent barium chloride, and the outgoing fluid was collected from the commencement of barium perfusion until the moment of onset of ventricular fibrillation. From the volume of this fluid the total amount of barium chloride which passed through the coronary system during that period was calculated. Allowance was made for the small amount of perfusate containing no barium, namely, that which occupied the short length of tube between the point of entry of the solution and the heart.

At the end of the experiment the heart was removed from the apparatus and weighed, and the number of milligrams of barium chloride per gram of heart tissue necessary to produce fibrillation was calculated.

In the earlier experiments the ventricular contractions were recorded graphically, but later it was found that the exact instant of onset of fibrillation could be determined more accurately by direct inspection.

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RESULTS

Table I shows the results of such experiments. It will be seen that the average amount of barium chloride per gram of heart tissue necessary to produce fibrillation was 1.87 mg. for the rabbit heart, 1.38 mg. for the cat heart, and 0.83 mg. for the dog heart. The rabbit heart, therefore, required the largest amount, the dog heart the least, and the cat heart was intermediate. This is in keeping with the observation of Garrey,[5] and others, that large hearts fibrillate more readily than small ones. Indeed, Garrey states that the tendency to recover from fibrillation is in inverse ratio to the tissue mass.

The cat heart is undoubtedly the most suitable for this type of experiment. The rabbit ventricles in some cases will not fibrillate at all, and the transition from coordinated beating to fibrillation is occasionally so gradual that it is difficult to identify the instant of onset. The dog heart, on the other hand, perhaps owing to the unsuitability of Locke's solution as a perfusate for large hearts, exhibits a tendency to spontaneous fibrillation and to various degrees of heart block which makes it unreliable as a standard.

The average amount of barium chloride per gram of cat heart necessary to produce fibrillation under these standardized conditions appears to be 1.38 mg. In order to ascertain whether this "fibrillation level" can be altered by drugs known to affect fibrillation induced by other means, we also investigated the effects of quinidine and digitalis on the onset of "barium" fibrillation. Quinidine has been found both experimentally[4] and clinically[6] to render the heart refractory to stimuli that would ordinarily throw it into ventricular fibrillation. To determine whether it would have a similar effect upon the fibrillation induced by barium, further experiments were performed, in which 0.75 mg. of quinidine was added to each liter of the Locke's solution perfused through the cat heart. After perfusion with as little as 20 to 50 c.c. of this solution, the heart beat more slowly and the strength of ventricular contraction increased. At this point, usually about five minutes after the onset of quinidine perfusion, barium chloride was introduced as described above, and the amount necessary to cause ventricular fibrillation was ascertained. The results are shown in Table II.

These experiments indicate that quinidine has a definite protective action against the ventricular fibrillation induced by barium, since the average amount of barium chloride required was raised from 1.38 to 2.52 mg. per gram of heart tissue. Moreover, the type of fibrillary movement was altered by quinidine. Ordinarily, after perfusion with barium, the cat's ventricular musculature exhibited fine, rapid, vermiform movements, but when the barium was preceded by quinidine, the fibrillary movements consisted of large, slow-moving, coarse undulations, sweeping over the ventricles.

TABLE I

AMOUNT OF $BaCl_2$ NECESSARY TO PRODUCE VENTRICULAR FIBRILLATION IN ISOLATED PERFUSED HEARTS

RABBIT					CAT					DOG				
NO.	C.C. $BaCl_2$	% $BaCl_2$	WT. OF HEART IN GM.	MG. $BaCl_2$ PER GM. HEART	NO.	C.C. $BaCl_2$	% $BaCl_2$	WT. OF HEART IN GM.	MG. $BaCl_2$ PER GM. HEART	NO.	C.C. $BaCl_2$	% $BaCl_2$	WT. OF HEART IN GM.	MG. $BaCl_2$ PER GM. HEART
1	5	0.2	5.5	1.8	1	14	0.3	21.5	1.96	5	37	0.3	83.5	1.3
2	6	0.2	6.5	1.8	2	8	0.3	17.5	1.37	6	24	0.3	99.5	0.72
3	5	0.2	6.0	1.7	3	7	0.3	15.0	1.40	7	29	0.3	90.5	0.90
4	6	0.2	6.5	1.8	4	13	0.3	14.5	2.68	17	50	0.3	115.0	1.3
5	did not fibrillate				5	10	0.2	17.0	1.18	18	30	0.3	80.0	1.14
6	did not fibrillate				6	15	0.2	25.0	1.20	19	30	0.15	97.0	0.48
7	4	0.2	5.4	1.8	7	8	0.2	12.5	1.28	20	60	0.10	79.0	0.76
8	did not fibrillate				8	12	0.2	26.5	0.91	21	24	0.2	65.5	0.74
9	7	0.2	5.4	1.8	9	7	0.2	14.5	0.97	22	18	0.2	65.5	0.54
10	6	0.2	4.9	2.4	10	10	0.2	12.0	1.67	23	59	0.2	108.0	1.1
11	3	0.2	4.2	1.4	11	7	0.2	13.0	1.08	24	32	0.2	111.0	0.58
12	5	0.2	4.5	2.2	12	10	0.2	16.0	1.25	25	66	0.15	86.0	1.1
13	5	0.2	5.3	1.8	13	8	0.2	16.0	1.00	26	40	0.15	94.0	0.63
14	6	0.2	6.2	1.9	20	9	0.2	13.0	1.38	27	84	0.15	163.0	0.56
15	5	0.2	5.5	1.9						28	36	0.15	81.5	0.66
			Average	1.87				Average	1.38				Average	0.83

TABLE II

AMOUNT OF $BaCl_2$ REQUIRED TO PRODUCE VENTRICULAR FIBRILLATION IN QUINIDINIZED HEARTS

NO.	C.C. $BaCl_2$	% $BaCl_2$	WT. OF HEART IN GM.	MG. $BaCl_2$ PER GM. HEART	COMMENT
Q1	13	0.2	8.6	3.0	Coarse fibrillation
Q2	17	0.2	14.1	2.4	Coarse fibrillation
Q3	22	0.2	18.2	2.4	Coarse fibrillation
Q4	10	0.2	16.5	1.2	Extremely coarse fibrillation
Q5	13	0.2	7.6	3.4	Extremely coarse fibrillation
Q6	34	0.2	15.6	4.4	Extremely coarse fibrillation
Q7	10	0.2	15.5	1.3	Extremely coarse fibrillation
Q8	14	0.2	16.0	1.8	
Q9	16	0.2	16.2	2.0	
Q10	16	0.2	9.7	3.3	
			Average	2.52	

The fact that quinidine increases the amount of barium chloride necessary to produce fibrillation leads us to believe that this method can be used to demonstrate elevation of the threshold for the initiation of fibrillary movements.

In order to find out whether the method could also detect a lowering of the fibrillation threshold, we performed similar experiments, using digitalis instead of quinidine. The cat heart was first perfused with Locke's solution containing 0.5 cat unit of digitalis per liter. As before, perfusion was continued until some irregularity in rhythm developed, or the contractile power of the heart was visibly altered, and then perfusion with barium chloride was started and the amount necessary to produce ventricular fibrillation determined.

Table III shows that after digitalis the average amount of barium chloride was decreased from 1.38 to 0.81 mg. per gram of heart tissue. It seems, therefore, that a lowered threshold for fibrillation can also be detected by this method.

TABLE III

AMOUNT OF $BaCl_2$ REQUIRED TO PRODUCE VENTRICULAR FIBRILLATION IN DIGITALIZED HEARTS

NO.	C.C. $BaCl_2$	% MG. $BaCl_2$	WT. OF HEART IN GM.	MG. $BaCl_2$ PER GM. HEART
D1	10	0.2	23.1	0.86
D2	11	0.2	26.9	0.82
D3	9	0.2	19.0	0.94
D4	5	0.2	14.0	0.72
D5	5	0.2	13.8	0.72
			Average	0.81

SUMMARY

By means of perfusion with barium chloride, the "fibrillation level," or tendency of the heart to fibrillate, may be measured, and the effects of drugs on this level may be studied.

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Department of Clinical Reports

PERICARDITIS WITH EFFUSION DUE TO THE MENINGOCOCCUS

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MENINGOCOCCIC infections present themselves, as a rule, in the form of acute, subacute, or chronic infections of the blood stream, with or without later metastatic localization in the meninges. The localization of meningococcic infection within the pericardium is distinctly rare, and a single case, presenting itself as a primary problem in pericardial effusion, is sufficiently unique to warrant a brief report.

Bettencourt and França,[1] in 1904, mentioned three cases of pericarditis complicating meningococcus meningitis, in two of which organisms were recovered by smear and culture. Weichselbaum and Ghon,[2] in 1905, reported an instance of meningococcic endocarditis and pericarditis, but the organisms were not recovered from the pericardium. In the same year, Lenhartz[3] recorded one case of proved purulent meningococcic pericarditis, and Elser,[4] in a review of 23 autopsies on patients with meningococcic meningitis, found five cases of pericarditis, the sacs containing 5 to 35 c.c. of seropurulent or purulent fluid. In two instances, organisms were seen in the smear and, in one instance, were recovered by culture. Duval,[5] in 1908, reported the case of a child, 7 years old, with meningitis and fibrinopurulent pericarditis, in which the organisms were obtained from the pericardial fluid by smear and culture. It is important to note that in all of the above cases of pericarditis there was an associated meningitis, and that all of the patients died.

Herrick,[6] in 1918, reviewed the essential features of 12 cases of meningococcic pericarditis which occurred during an epidemic of 280 cases of meningitis and pointed out that pericarditis is usually a complication of serious meningococcic sepsis. Six patients presented effusions varying in amounts from 30 c.c. to 640 c.c.; the remaining six were of the "dry" type. In four cases, the diagnosis was made during life, and two of the patients recovered. Of those who recovered, one had the largest effusion, 640 c.c. of purulent fluid, in which organisms were demonstrated by smear and culture; the other presented only an audible pericardial friction rub. Zuccola,[7] in 1929, reported an instance of a young man with meningococcemia and meningitis from whose pericardial sac a few cubic centimeters of purulent fluid were removed, but no organisms were identified. Recovery followed serum therapy. Trace and Berkovitz,[8]

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in 1931, recorded the case of a boy, aged 13 years, with meningococcic meningitis, who developed a pericardial friction rub on the fifth day of his disease. Pericardial paracenteses on two occasions yielded small amounts of seropurulent fluid containing a few intracellular, Gram-negative diplococci, but no organisms were grown on culture. Recovery followed intraspinal, subcutaneous, intramuscular, and intrapericardial injection of serum. In his review of the subject of meningococcic myocarditis, Saphir,[9] in 1936, mentioned one case in which the pericardial sac contained 150 c.c. of seropurulent fluid, but bacteriologic examination of the fluid was not reported. The occurrence of pericarditis in meningococcic infections is mentioned by several authors,[10, 11, 12] but little comment is made except by Adshead,[10] who ascribed the pericarditis to serum therapy in four cases, in all of which the patients recovered. It is interesting that several reviews of pericarditis,[13, 14, 15] meningococcemia,[16] and the newer reference texts[17, 18] fail to mention the meningococcus as an etiologic agent in pericarditis.

CASE REPORT

History.—R. W., a white, 32-year-old minister, entered the hospital March 30, 1938, with the primary complaint of dull, constant, aching substernal pain, of two weeks' duration. The family, marital, and past histories were noncontributory. In general, his health always had been good. The history of his present illness revealed that he was in good health until 16 days prior to entry, when he had two impacted wisdom teeth removed. He felt perfectly well until the second postoperative day, when he noted that the left side of his neck ached and was mildly stiff; this remained so for about two days. Four days after the operation he developed dull, constant, aching substernal pain. Six hours after the onset of chest pain, he was seen by his physician, who discovered that his temperature was 102° F., by mouth. Sulfanilamide and analgesics were administered. He remained in bed for about two days, his fever subsided, and the pain disappeared. He then arose and resumed his normal duties, but he felt somewhat weak; however, he was able to play eighteen holes of golf on three of the next six days with but slight dyspnea. Three days prior to his entry there was a return of the dull aching substernal pain, and a roentgenogram of the chest showed cardiac enlargement. He resumed complete bed rest until admission to the hospital, to which he came because of pain, low-grade fever, and moderate dyspnea.

Physical Examination.—The temperature was 38.4° C., the pulse rate, 84; the respiratory rate, 26; and the blood pressure 110/70. The patient was a slender, fairly well-developed, intelligent, cooperative young white man, appearing ill, with moderate dyspnea and orthopnea. No petechiae or skin eruptions were seen. There was no generalized lymphadenopathy. The eyes and ears showed no abnormalities. The nasal septum was deflected to the left, with considerable obstruction to breathing space. The existing teeth were in good condition; no pyorrhea was present. The neck veins showed moderate engorgement; the trachea was in the midline; the thyroid gland was not enlarged. The lungs showed dullness and diminished breath sounds at the right base, with moist crepitant râles bilaterally. The heart was markedly enlarged to the right and left, with obliteration of the pericardial angle on the right. The apex impulse was not seen or felt. The heart sounds were distant and much diminished in intensity; no murmurs were heard. The rhythm was normal. The peripheral vessels showed no thickening. The pulse was of small volume, with a distinct paradoxical character both to palpation and

manometric readings. A tender liver was palpated about five centimeters below the right costal margin. The spleen was not felt, and no ascites was demonstrated. Genital and rectal examinations showed nothing remarkable. The extremities were grossly normal. No edema was noted.

Laboratory Data.—The hemoglobin was 13 grams; the erythrocyte count, 3,780,000; the color index, 1.1; and the leucocyte count 9,400. The differential leucocyte count showed polymorphonuclear leucocytes, 84 per cent; basophils, 2 per cent; monocytes, 2 per cent; large lymphocytes, 3 per cent; and small lymphocytes, 9 per cent. The sedimentation rate was 26 mm. per hour, corrected. Repeated urinalyses and stool examinations were negative. Roentgenologic examination of the chest showed generalized pulmonary congestion, with fluid at the base of the right lung and enlargement of the cardiac silhouette both to the right and left. The electrocardiogram showed normal sinus rhythm, a rate of 104, no abnormal axis deviation, normal P-R and QRS intervals, borderline voltage, with a maximum deflection of plus 6 in Lead II, an isoelectric to inverted T_1, an upright T_2 and T_3; and a normal precordial lead. The borderline voltage, plus the T-wave inversion, was entirely consistent with pericardial disease. The blood culture was negative. Tuberculin tests were negative.

Course in the Hospital.—During the first few hospital days his temperature persisted at a level of about 38° C. On the fourth day pericardial paracentesis was performed; 200 c.c. of thin, serosanguineous fluid were removed, and replaced by 150 c.c. of air. The fluid clotted quickly; its specific gravity was 1.030. A cell count revealed 2,550 leucocytes per cmm., of which 8 per cent were polymorphonuclear neutrophiles, and 92 per cent, lymphocytes. Smears revealed Gram-negative diplococci. The organisms were grown in culture and identified as meningococci (*N. intracellularis*). The agglutination titer, using the patient's serum and organisms, was 1-40. Dramatic improvement followed the paracentesis. His temperature remained normal for six days, the pulmonary congestion quickly receded, and the venous pressure diminished. A teleoroentgenogram showed a thickened pericardium enclosing fluid and air. On the tenth hospital day an unsuccessful pericardial paracentesis was performed. Two days later his temperature rose to 39° C., consolidation appeared in the lower lobe of the right lung, and two successive blood cultures were positive for *N. intracellularis*. Sulfanilamide administration was begun immediately, in doses of 4.8 gm. per day for a period of eighteen days, with improvement manifested by the gradual return of his temperature to normal and the disappearance of all signs of pericardial effusion and lung consolidation. A thrombophlebitis of the right leg, which developed during this period, also cleared up. Blood cultures became negative and remained so throughout his hospital course. Cultures from the nose, mouth, and throat were negative for *N. intracellularis*. On the fortieth hospital day, after five days of normal temperature, a fever of 38° C. to 39° C. reappeared. Antimeningococcic serum was administered in a quantity of 165 c.c. over a six-day period; it was given intramuscularly because of violent reactions to intravenous injection. Serum sickness developed, but no other significant response to serum therapy was noted. Sulfanilamide was given again on the forty-seventh hospital day and continued for one week. His temperature fell to normal, and remained so until his discharge on the fifty-sixth hospital day. By this time all symptoms and signs had disappeared, and fluoroscopic examination of the heart and lungs showed nothing abnormal. Immune antibodies developed in the patient's blood, as evidenced by agglutinins in a serum dilution of 1-1280, bacteriolysins in a serum dilution of 1-100, and marked opsonophagocytosis. The patient has been followed for 7 months since his discharge by his own physician, who reports his health to be excellent and his heart normal to physical examination.

DISCUSSION

This case represents a rare instance of meningococcic infection producing typical pericardial effusion with cardiac tamponade. There was no history to suggest meningococcemia or meningitis as a preliminary to the development of pericarditis. This is particularly interesting, for in the previously reported cases there has been, almost invariably, an accompanying meningitis. The usual portal of entry in meningococcic infections is believed to be the upper respiratory passages, and it is possible that the organisms were introduced into the blood stream at the time he had his teeth extracted,[19] with subsequent metastatic localization in the pericardium. This was probably the only focus of infection at the time of admission. Cultures from the nose, mouth, and throat were all negative for meningococci. It is noteworthy that pericardial paracentesis yielded thin, serosanguineous fluid containing a small number of cells, largely lymphocytes, and organisms which were demonstrated by smear and culture. The blood culture, while initially negative, became positive for several days following a second and unsuccessful paracentesis. It is conceivable that the organisms gained entrance to the blood stream at this time. Following the removal of the effusion, with subsequent relief of cardiac tamponade, the problem in therapy shifted from one primarily cardiac to that of meningococcemia. Sulfanilamide alone was ineffective in controlling the disease, but when it was given in conjunction with antimeningococcic serum recovery was complete. The development of immune antibodies in high titer in the blood stream is supportive evidence of cure.

Meningococcic pericarditis produces no symptoms or signs distinctive of the causative organism. While it is usually a feature of the late period of the acute stage of the disease,[6] and is generally seen with meningitis, it need not necessarily be associated with meningococcemia, meningitis, or other severe complications. The pericarditis may be evidenced by signs varying from a simple friction rub to those of a large effusion, which may be serous, purulent, sanguineous, or combinations of these, and may contain predominantly lymphocytes or polymorphonuclear leucocytes.

Treatment consists of paracentesis, if effusion is present, sulfanilamide, and antimeningococcic serum, which should be administered intrapericardially as well as intravenously, as first suggested by Herrick. The mortality in the reported cases is definitely high, but this is more likely attributable to the preceding serious infection than to the pericarditic complication. It is suggested that in those cases of pericardial effusion in which organisms are not easily demonstrated, care should be taken to rule out meningococcic infection.

CONCLUSION

1. An instance of meningococcic infection producing pericardial effusion with cardiac tamponade is reported.

2. Complete recovery followed pericardial paracentesis and treatment with sulfanilamide and antimeningococcic serum.

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Department of Reviews and Abstracts

Selected Abstracts

Katz, L. N., and Lindner, E.: Quantitative Relation Between Reactive Hyperemia and the Myocardial Ischemia Which It Follows. Am. J. Physiol. **126**: 283, 1939.

The quantitative effect on coronary flow of different periods of myocardial ischemia was observed in an isolated preparation of the dog heart with ventricles fibrillating. Blood flow through the forelimb of the same animals was studied simultaneously under the same conditions. In this preparation coronary flow is determined entirely by active changes in the coronary vessels.

In the heart, correlation of the components of the ischemic periods, with those of the subsequent hyperemic periods and analysis of the relationships found, led to the following conclusions:

1. In this preparation, the coronary blood supply is greater than that necessary to meet myocardial needs.

2. The hyperemia due to the ischemia is more than adequate to make up for the myocardial deficit acquired.

3. The cause of the hyperemia seems to be an easily diffusible dilator substance which is eliminated in the presence of oxygen.

4. The degree of hyperemia not only varies with the duration of the ischemia and hence with the accumulation of the dilator substance, but also with the responsiveness of the coronary vessels to this substance.

The coronary vessels are decidedly more reactive to ischemia than are the limb vessels.

The importance of reactive hyperemia as a mechanism operating to compensate for any inadequacies in coronary flow in the intact animal is emphasized, and the bearing of these data on reactive hyperemia in other vascular beds is suggested.

AUTHORS.

Christianson, Oscar O.: Observations on Lesions Produced in Arteries of Dogs by Injection of Lipids. Arch. Path. **27**: 1011, 1939.

Lesions were produced in arteries of dogs by injecting into the media of the abdominal aorta and femoral arteries, human fat alone or mixed with fatty acids, calcium soaps, or cholesterol. The severity and chronicity of the lesions varied with the acidity and speed of dispersal of the fat mixture. Human fat and fatty acids produced marked acute inflammatory lesions which healed rapidly because the lipids absorbed readily. Human fat mixed with calcium soaps or cholesterol was absorbed slowly and caused a chronic lesion. In the formation of arteriosclerotic lesions in man the infiltrating lipids as well as cholesterol may be important in producing fibrous tissue.

Most of the medial lesions produced disruption or splitting of the internal elastic lamina and development of intimal plaques. Thus intimal lesions were secondary to medial lesions simulating the early changes described in arteriosclerosis in man. Injuries of the media may be important in the production of secondary intimal changes which predispose to the deposition of lipids in the early lesions of arteriosclerosis.

NAIDE.

Hallock, Phillip: Lactic Acid Production During Rest and After Exercise in Subjects With Various Types of Heart Disease, With Special Reference to Congenital Heart Disease. J. Clin. Investigation **18**: 385, 1939.

An increased concentration of lactic acid in the venous blood is evidence of an inadequate supply of oxygen to the tissues.

There is only a slight increase of lactic acid in the blood following mild exercise in normal individuals, an average increase of about 2 mg. per 100 c.c. of blood above the resting value. The normal upper limit of concentration of venous blood lactic acid following our exercise test did not exceed 21 mg. per 100 c.c. of blood.

The blood lactic acid studies show that tissue anoxia is not present at rest in patients with congenital heart disease, either in the presence or absence of cyanosis.

Following mild exercise there is a definitely abnormal rise of blood lactic acid in the cyanotic group of congenital heart disease, indicating a greater liability to the development of tissue oxygen deficit after even slight physical exertion.

The presence of cyanosis and polycythemia in congenital heart disease does not necessarily indicate that oxygen deficit will develop following mild exertion for no significant rise of lactic acid level occurred in a case of morbus caeruleus.

Following mild exertion, a definitely abnormal rise may occur in some acyanotic cases of congenital heart disease, but the rise is not as great on the average as in the cyanotic group.

When dyspnea follows mild exercise the presence of tissue oxygen want may be assumed to be present regardless of what specific cardiac defect is ultimately responsible.

AUTHOR.

Gubner, Richard, Schnur, Sidney, and Crawford, Hamilton: The Use of CO_2 Inhalation as a Test of Circulation Time. J. Clin. Investigation **18**: 395, 1939.

CO_2 inhalation may be employed clinically to estimate circulation time. The CO_2 test measures "left heart" time (lung to respiratory center). Its advantages are that it is a physiologic respiratory stimulant; it is entirely harmless; the effect is transitory; it does not require injection, and it may be used repeatedly in the same subject.

The circulation time, by this method, is prolonged in heart disease commensurate with the degree of left heart failure. Normal values range from 5 to 10 seconds and correspond closely to the expected results according to the cyanide and ether times.

AUTHORS.

Gold, Harry, Kwit, Nathaniel T., Otto, Harold, and Fox, Theodore: On Vagal and Extravagal Factors in Cardiac Slowing by Digitalis in Patients With Auricular Fibrillation. J. Clin. Investigation **18**: 429, 1939.

There is no general agreement regarding the role of the vagus in the ventricular slowing by digitalis, some maintaining that the drug acts mainly on conduction directly, and others, that its action is mediated chiefly or wholly through the vagus.

In the present investigation on patients with auricular fibrillation the authors found, as others have, that paralytic doses of atropine always cause some acceleration of the ventricle which has been slowed by digitalis, and that this effect varies from slight acceleration to complete abolition of the slowing.

They have observed, however, that if the doses of digitalis are large enough, atropine cannot prevent digitalis from producing marked slowing of a rapid ventricle (to 100 a minute or slower).

In digitalized patients with auricular fibrillation, the ventricle is maintained at a slow rate usually by the summation of two factors: one, a vagal factor (abolished by atropine), and two, an extravagal factor (not abolished by atropine).

In the average case, the vagal factor predominates in the slowing of the ventricle after moderate doses of digitalis, while the extravagal factor predominates after large doses.

Which of the two factors (vagal or extravagal) will dominate in the control of the slowed heart rate depends, therefore, upon the degree of digitalization. Contrary to statements found in the literature, the results show that it is not a matter of individual peculiarity, the degree of heart failure, or the length of time the heart has been under the influence of digitalis.

The discordant views in the literature regarding the role of the vagus and the factors which alter its role, in slowing of the ventricle in auricular fibrillation, arise from the failure to make adequate observations on the effect of maximum doses of atropine after different doses of digitalis in one and the same subject.

AUTHORS.

McMichael, John: Hyperpnea in Heart Failure. Clin. Sc. 4: 19, 1939.

The best available method of standardizing measurements of pulmonary ventilation is by the use of a ventilation equivalent. The ventilation equivalent for oxygen is liable to a considerable error, especially with fluctuations in the respiratory quotient. The ventilation equivalent for CO_2 is less liable to fortuitous changes. Normal values of these functions are surveyed statistically.

The standard error of the acetylene method of determining cardiac output is assessed as 4.5 per cent from 85 checked determinations.

In heart failure there is no great correlation between hyperpnea and vital capacity. There is, however, a close correlation between cardiac output and hyperpnea.

When the general systemic blood flow is lowered in cardiac failure, there is good reason to believe that the cerebral blood flow is not depressed to the same degree.

Consideration of published and personal data on the jugular venous oxygen content supports the hypothesis that the cerebral blood flow is subnormal in hyperpneic cardiac subjects.

AUTHOR.

De Boer, S.: Researches on the Electrocardiogram. Cardiologia 2: 292, 1938.

A polemical review of the author's work is assembled in order to refute Lewis' theory of limited potential differences and also Craib's deductions regarding monophasic curves. The author advocates the interference theory.

KATZ.

Burger, R.: The Electrical Field of the Heart. Cardiologia 3: 56, 1939.

A lead can be taken from the surface of the body as a whole using the metal tub bath with a metal lead as the W electrode (bath electrode), and using this as an indifferent electrode. This was employed in five normal cases. It was found that the decrease due to the short-circuiting effect of the water on the potential

differences of the extremity leads was a constant percentage at different instances of the cardiac cycle. This method is used to deal at great length with the question of what is an "indifferent electrode," a "zero-potential electrode," and a "unipolar lead."

KATZ.

Burger, R., and Wuhrmann, F.: The Electrical Field of the Heart. Cardiologia 3: 139, 1939.

A method is suggested of determining the electrical field of the heart at different instants of the heart cycle. Such diagrams are called diagrams of potential differences. These are obtained by measuring the potential at a particular instant in the heart cycle of many points in the body especially on the precordium, back, and in the esophagus. A relatively complex mathematical derivation is used. Comparison made by this means and by the vector diagram ordinarily used shows that the location and movements of potentials can be followed more accurately by the authors' methods especially since their method gives the individual components of the electrical field and not only the resultant.

KATZ.

Cowan, John: Some Disturbances of the Rhythm of the Heart. Brit. Heart J. 1: 3, 1939.

Alterations in the rhythm of the heart, as isolated signs, are not necessarily of serious significance.

James Mackenzie stated (1912) that *sinus irregularity* in a healthy individual was a normal occurrence, and many observers have subsequently confirmed the accuracy of his dictum. It is true that *sinoauricular block* may, as shown in some of the cases which we have collected, be accompanied by serious symptoms, but the subsequent history of these patients shows that, in the absence of signs of cardiac disease, the prognosis from the cardiac standpoint is quite good. Any danger lies in the nature of the nervous disorder which occasions it.

The occurrence of *extrasystoles, per se,* has not any sinister significance. It is true that if they recur rapidly for long periods the mere rapidity of the cardiac contractions may produce cardiac failure, but, in the absence of signs of cardiac disease, any cardiac symptoms rapidly pass as soon as the normal rhythm is restored. A man, who died from paralysis agitans at the age of 75, had been liable to attacks of paroxysmal tachycardia from the age of 18 and had lived a very strenuous life for many years.

The prognosis in cases of *nodal rhythm* depends, as in sinus irregularity, upon the nature of its cause. The outlook is serious if it is due to myocardial lesions, but good if it is due to nervous causes.

The occurrence of *auricular fibrillation* is generally a signal of impending danger, but the exceptions to the rule are fairly numerous. Cases have been reported where the arrhythmia persisted for ten or even twenty years. One of my patients bore a child safely although her auricles had been in fibrillation for at least three years. The irregularity is not the important factor in the failure. The danger lies in the frequency of the ventricular contractions or in the continued activity of the cause of the irregularity. Fibrillation may be due to several causes; pathologic lesions in the auricular muscle, of chronic or acute character; autointoxications, as in Graves' disease; poisons introduced from without (digitalis, anesthetics, coal-gas poisoning, etc.); physical stresses; and perhaps to disturbances of the nervous control of the heart (Cowan, 1929). The cause may be permanently or temporarily in action. The prognosis follows the cause.

Heart block and bundle branch block repeat the story. As they are most frequently due to myocardial disease the prognosis is, as a rule, serious, but many patients live in fair health for many years. Again the danger lies in the rate of the ventricular contractions, or in the character of the process which has disturbed the rhythm of the heart.

AUTHOR.

Peel, A. A. Fitzgerald: The Significance of Electrocardiograms Showing a "Second Positive Wave of QRS" in Lead III. Brit. Heart J. 1: 86, 1939.

Organic heart disease is more common in patients whose electrocardiograms show a "second positive wave of QRS_3" than in the material from which these cases were collected (82 against 72 per cent). Many of these electrocardiograms show some other significant abnormality, in which case organic disease is always present, and the mortality since 1928 to 1933 has been 90 per cent.

Organic lesions are much more frequent in patients whose sole electrocardiographic abnormality consists of a "second positive wave of QRS_3" than in patients whose electrocardiograms are completely normal (70 per cent against 43 per cent). The increase is due to a greater number with coronary disease, hypertension, or arteriosclerosis (42 per cent against 8 per cent).

Where it has been possible to fix the time of appearance of the "second positive wave of QRS_3," this has occurred when an active pathologic process was affecting the myocardium. In seven out of eight cases in which it ultimately disappeared, the patient's capacity for effort improved, at least temporarily.

When a "second positive wave of QRS_2" is the only electrocardiographic abnormality, the shape of the complex is important for diagnosis and prognosis, and its breadth gives further assistance in prognosis.

As regards the shape of the complex, the height of the initial R is the determining factor. When this was prominent, deflection exceeding 2 mm. in height, organic disease was always present; and the mortality in cases with an otherwise normal electrocardiogram was 50 per cent. When the initial R was a small deflection of less than 2 mm. in height, the incidence of recognizable organic disease was only 62 per cent, and the mortality in cases with an otherwise normal electrocardiogram was only 12 per cent.

The breadth of QRS gives little help in diagnosis, but is of great importance in prognosis. The mortality rises steadily from 22 per cent with a QRS below 0.08 sec., to 55 per cent at 0.08 sec., and to 72 per cent above 0.08 sec. These mortality figures are almost identical with those found in healing with another series of electrocardiograms where the abnormality was a "large Q_3." The significance of the breadth of QRS, therefore, apears to be independent of the nature of any abnormality which may be present.

AUTHOR.

Chamberlain, E. Noble, and Hay, J. Duncan: The Normal Electrocardiogram. Brit. Heart J. 1: 105, 1939.

To determine the limits of physiologic variation in the electrocardiogram and any changes that might occur with age, 302 normal subjects have been investigated. Each was subjected to a rigorous examination, including blood pressure readings and Wassermann reaction. The following points are deemed worthy of emphasis.

The P wave was often flat or scarcely perceptible in Lead I and occasionally had a split or broad summit. A few examples of inversion P_2 were seen.

The R wave varied within wide limits in its amplitude, and slight notching of the descending limb was not uncommon.

The S wave, although usually well defined, may slope gradually into the R-T segment.

True S-T deviation was so rare and so minute that it must be regarded with great suspicion, but peculiarities in the formation of the S-T interval were very common and must not be confused with genuine S-T deviation.

Slight degrees of notching and of low voltage in the QRS complex in Leads I and II were not common. The types of record found can be seen better by inspection of the illustrations than by description.

Right axis deviation in a pronounced form was uncommon even in young persons, while left axis deviation occurred quite frequently at all ages, increasingly so in the later decades where it was found in one-sixth of all cases.

Inversion of T was never found in Lead I, but inversion of T in both Leads II and III was present in four cases. The former must be considered as pathologic whenever it occurs, and the latter as suspicious. Inversion of T in Lead III only was present in 29 per cent of the total 302 cases, and considerable variation in the shape of the wave was recognized.

The only unusual finding as regards time intervals was the occurrence of a few cases where the P-R interval was 0.22 second.

Age variations were slight, the most important being an increase in the left avis deviation in the later decades of life.

AUTHORS.

Wood, Paul, and Selzer, A.: A New Sign of Left Ventricular Failure. Brit. Heart J. **1**: 81, 1939.

A widened P wave of low voltage, usually bifid or flat-topped, has been found in association with left ventricular failure in cases of hypertensive heart disease and of aortic incompetence.

It is suggested that this P wave results from left auricular stress.

AUTHORS.

Bruetsch, Walter L.: The Histopathology of the Psychoses With Subacute Bacterial and Chronic Verrucose Rheumatic Endocarditis. Am. J. Psychiat. **95**: 335, 1938.

The involvement of the brain during the course of an endocarditis is not uncommon. From an etiologic point of view two types of psychosis with endocarditis can be distinguished.

(1) Psychoses with subacute bacterial endocarditis, terminating fatally within several months. Histologic examination reveals numerous miliary abscesses and masses of cocci in capillaries of the brain cortex and in other organs.

(2) Psychoses with chronic rheumatic endocarditis. The patients in this group may present any reaction type. Some of the cases were diagnosed as dementia praecox, other cases as manic-depressive or involutional psychoses. A 62-year-old patient with a recent rheumatic infarction of the parietal-occipital region was classified as senile psychosis.

The anatomic findings in the brain consisted of small or large areas of infarction, being usually the result of rheumatic-endarteritic changes. Or the brain was grossly normal, but microscopic examination disclosed numerous acellular areas, an occasional granuloma, and small connective tissue scars. In one patient with a psychosis of short duration a rheumatic encephalitis was present.

AUTHOR.

Bruetsch, Walter L.: Chronic Rheumatic Brain Disease as a Cause of Mental Disorders. Ztschr. f. d. ges. Neurol. u. Psychiat. **166**: 4, 1939.

The material on which this work is based comprises 475 complete autopsies, performed in an institution for mental diseases, in which particular attention was given to the presence of rheumatic valvular heart disease. The frequency of chronic rheumatic endocarditis among mental patients is given as 4 per cent. This finding is of particular interest, since obvious rheumatic manifestations, in particular polyarthritic symptoms, are rarely seen in mental hospitals. Histologic examination of all the organs of these patients revealed the interesting fact that the long-continued rheumatic infection had not only involved the heart, but also the brain and other organs, such as kidneys, spleen, pancreas.

The fundamental rheumatic lesion in the brain consisted of a vascular process of an obliterating endarteritic type with subsequent degeneration in the parenchyma. The anatomic findings seem to suggest that in a great majority of mental patients with chronic rheumatic valvular disease, a rheumatic brain involvement may be present.

The relation of rheumatic infection to arterial disease was first emphasized by Krehl who described in 1890 rheumatic endarteritis of the small myocardial arteries. In more recent years (1926) von Glahn and Pappenheimer and others demonstrated specific rheumatic lesions in the vessels of all the internal organs. They found rheumatic-endarteritic changes in the lungs, kidneys, pancreas, ovaries, and testes. If in this process the cerebral vessels take part, changes in the nervous parenchyma will occur. For this condition the term of chronic rheumatic brain disease was used.

AUTHOR.

Gross, Harry, and Handler, Bernard J.: Sclerosis of the Superior Vena Cava in Chronic Congestive Heart Failure. Arch. Path. **28**: 22, 1939.

The superior venae cavae of twenty-one persons showing chronic congestive heart failure were studied and compared with those of a group showing hypertrophy of the right side of the heart without failure and with those of another group in whom there was no cardiac lesion at all.

In persons with chronic congestive heart failure associated with increased tension in the right side of the heart and in the superior vena cava, sclerosis of the superior vena cava is a common finding.

Histologically, the sclerotic process in the superior vena cava is characterized by hypertrophy of all the coats of the vein, most marked in the muscular layer of the media. These alterations are thickening and scarring of the intima, splitting and reduplication of the internal elastic membrane, and widening of the media with hypertrophy of the muscle cells and increase of collagen. Eventually, from increased tension and impairment of nutrition, fragmentation, and replacement of muscle fibers occur.

Involvement of the superior venae cavae in persons not having congestive heart failure was slight and infrequent, and in not a single vein were all the coats of the vessel involved. Medial hypertrophy, which was so constant and marked in the superior venae cavae of the group who died in congestive heart failure, was an infrequent occurrence.

Phlebosclerosis and arteriosclerosis are similar in morbid anatomy and pathogenesis. The pathogenesis of sclerosis of the superior vena cava appears to be prolonged increase of intravascular pressure.

AUTHORS.

Jones, Noble W., and Rogers, Arthur L.: Chronic Infection and Atherosclerosis. Med. J. Australia **1**: 851, 1939.

The observation that compensation could not be restored in two patients with congestive heart failure until tonsillectomy and radical sinus surgery was performed in one patient and drainage of infection in the common bile duct in the other, led the authors to make special histologic and bacteriologic studies of the arteries in the first patient and subsequently in other atherosclerotic patients. In the sinus tissue of the first patient the arterioles lying in the depth of the membranes were noteworthy because of an almost universal subacute arteritis and a thrombotic process which occluded many of their lumina. Scattered diffusely throughout the walls of the vessels, and in the thrombi also, were many microorganisms in the form of diplococci, as revealed by specially stained sections. This picture was at marked variance with the arterioles in the sinus tissues removed from patients suffering from chronic arthritis or asthma, in which the blood vessels were slightly or not at all affected. The arteries in the walls of gall bladders removed from atherosclerotic patients were found to be in an inflammatory state, with diplococci present in the involved areas.

These facts suggested a relationship to distant thromboses and led the authors to study eleven unselected patients who died from acute coronary thrombosis. In all, the same general histologic picture of subacute arteritis with atheromatous degeneration was noted, and also in each one microorganisms in the form of diplococci were found in the tissues. In a few instances single and short chain cocci were seen. In these eleven cases there were associated chronic cholecystitis three times and a severe grade of pericemental infection and chronic sinus disease each twice.

The coronary arteries of children and patients with essential hypertension did not reveal any inflammatory changes, nor could microorganisms be found in them.

The inflammatory reaction and diplococci were demonstrated in the arterial wall of arteries in one patient with thromboangiitis obliterans and in a patient with periarteritis nodosa.

In conclusion the authors point out that in certain instances of atherosclerotic heart disease there exists a clinical relation to infection and that the removal of the latter beneficially affects the course of the former. In addition they were able to demonstrate microorganisms in the walls of all atherosclerotic vessels in which a careful search was made.

NAIDE.

Stead, Eugene A., Jr., and Kunkel, Paul: Mechanism of the Arterial Hypertension Induced by Paredrinol (a-N-Dimethyl-p-Hydroxyphenethylamine). J. Clin. Investigation **18**: 439, 1939.

Paredrinol (a-N-dimethyl-p-hydroxyphenethylamine) produces in normal subjects a type of acute arterial hypertension that closely resembles that observed in disease. The tendency to a slower heart rate, the vigorous apex impulse, the loud heart sounds, and the hypertension itself are the only outstanding abnormalities produced by the administration of the drug.

This hypertension differs greatly from that produced by epinephrine.

The arterial blood pressure response in different subjects, and in the same subject on different days, varies greatly. The average duration of the hypertension after the intramuscular injection of 25 mg. of paredrinol is one hour.

The blood flow in the dilated hand is moderately decreased. The spontaneous fluctuations in vasomotor tone in the hand and foot are decreased. The venous tone in the hand is increased. The venous pressure is increased by from 30 to

40 mm. of water. The T waves in the electrocardiogram become higher. These changes are usually not great enough to be detectable unless the resting values for the particular subject are known.

There is no significant change in blood flow in the foot, forearm, and calf. The cardiac output, circulation time, and basal metabolism are not significantly altered.

The decrease in heart rate results from an increase in vagal tone brought about by stimulation of the carotid sinus and aortic nerves, since if the vagal effect is removed by atropine, paredrinol causes an increase rather than a decrease in heart rate. When atropine is given before the injection of paredrinol the arterial pressure, particularly the diastolic, rises to higher levels than after paredrinol alone.

The combination of nitrite and tilting to the upright position pools sufficient blood to reduce the paredrinol hypertension to normal. Thus, if the arterial blood pressure rises to alarming heights, or if headache develops, the hypertension can be rapidly and permanently reduced.

The peripheral blood flow in subjects with arteriosclerosis and in subjects who have had a preganglionic sympathectomy is not increased by raising the arterial pressure head with paredrinol.

The hypertension produced by paredrinol may result from either or both of the following mechanisms: 1. A primary increase in peripheral resistance from a direct vasoconstrictor effect on the minute vessels (arterioles, capillaries, venules); 2. A primary increase in venous tone and an emptying of the splanchnic reservoirs, causing increased venous return to the heart and a secondary increase in peripheral resistance.

AUTHORS.

Katz, L. N., and Jochim, K.: Observations on the Innervation of the Coronary Vessels of the Dog. Am. J. Physiol. **126:** 395, 1939.

A method is described for determining the action of the sympathetic and parasympathetic nerves on the caliber of the coronary blood vessels in a preparation consisting of an isolated head and heart with fibrillating ventricles.

Evidence is presented showing that in the dog:

1. The vagi carry only cholinergic coronary vasodilator fibers which are tonically active. No evidence was obtained of cholinergic coronary vasoconstrictor fibers.

2. The stellate ganglia send to the heart adrenergic coronary dilator and adrenergic coronary constrictor fibers, both of which are tonically active.

3. The tonic action of the sympathetic nerves is predominantly vasoconstriction.

AUTHORS.

Perlow, Samuel, and Halpern, S. Sherman: Surgical Relief of Pain Due to Circulatory Disturbances of the Feet. Am. J. Surg. **45:** 104, 1939.

Operative peripheral nerve block has been a satisfactory method of relieving pain in many patients with peripheral vascular disease. However, occasional sloughing ulcers occur at the site of incision and in some cases the poor circulation causes the surgeon to hesitate to perform nerve block. In a search for another simple pain-relieving measure, it was found that injection of procaine in oil solutions into peripheral nerves induced anesthesia for one to forty days. Anesthesia involved the sympathetic, sensory, and motor fibers. No harmful results were produced by the procaine in oil injection into the nerve. The anesthesia is similar to that obtained by peripheral nerve block with alcohol or crushing but is not so long lasting. However, it can be repeated as desired and has the advantage of not requiring an operative incision.

NAIDE.

Book Reviews

ATLAS DE PHONOCARDIOGRAPHIE CLINIQUE: By A. Calô, Assistant étranger à la Faculté de Médecine de Paris. Membre correspondant étranger de la Société Française de Cardiologie. 104 pages, 150 illustrations, 60 francs, Paris, 1938. Masson et Cie, Editeurs, Libraires de L'Academie de Medecine, 120 Boulevard Saint Germain, Paris, France.

During the last few years there has been a great revival of interest in the graphic registration of heart sounds and murmurs, with the result that several makers of electrocardiographs have placed on the market apparatus for recording a sound tracing simultaneously with an electrocardiogram. Many physicians have not found the records as useful as they had anticipated, however, largely because they do not know how to interpret the graphs. For this reason a book that contains a large number of sound records and describes their salient features is to be welcomed.

This atlas opens with a brief discussion of the method employed and the technique required to obtain tracings free of unwanted vibrations. This is followed by classification into logical groups of the different sounds and murmurs arising from the heart, and a fairly detailed discussion concerning their origin, time of occurrence in the heart cycle, duration, and other important characteristics.

The second part of the atlas, which occupies three-quarters of the book, is devoted to the reproduction and description of sound records from a large group of patients, including several with normal heart sounds. Tracings that illustrate the common murmurs encountered in patients with valvular heart disease and congenital heart disease are shown, in addition to many other graphs depicting alterations in the heart sounds and various types of gallop sounds. The presentation is very complete because in each instance sound tracings from at least three points on the chest, i.e., the cardiac apex and the aortic and pulmonic areas, are shown, and each sound record is taken simultaneously with one lead of the standard electrocardiogram. The majority of graphs also include a simultaneous arterial pulse tracing. On the page opposite the graphic records, the author gives a brief summary of the history and physical examination of the patient whose records are shown, together with an orthodiagram and an interpretation of the standard electrocardiogram and the sound tracings.

The tracings are very well reproduced throughout the atlas, and, although very low frequency oscillations seem to dominate many of the records, these vibrations are seen to occur quite constantly in every heart cycle, indicating that they are not artifacts. The author emphasizes that many of the low frequency vibrations that appear on the records would be heard with difficulty, or might be entirely inaudible. Attempts are made to estimate from the tracings the fundamental frequency in the heart sounds and murmurs. The reviewer does not feel that such frequency determinations are worth while, because the results obtained depend to a very large degree on the nature of the microphone and amplifier employed in the recording system.

An excellent bibliography is provided, and the atlas should be of great value to many physicians desiring information on this subject.

FRANKLIN D. JOHNSTON.

CARDIOVASCULAR DISEASE IN GENERAL PRACTICE: By Terrence East, M.A., M.D., F.R.C.P. (London), Physician and Physician in Charge of Cardiological Department, King's College Hospital, London. 206 pages, 43 illustrations, $3.50, 1939, H. K. Lewis and Co.

This book of approximately two hundred pages is an extremely useful summary of the knowledge relating to heart disease that is most essential for the general practitioner, or indeed for the specialist in this field. It might be more accurately entitled "Heart Disease in General Practice," inasmuch as only one short chapter is devoted to vascular diseases; the three selected for discussion are thromboangiitis, Mönckeberg's sclerosis, and Raynaud's syndrome. It is probably true in England, as it is in the United States, that very few "heart specialists" are also specialists in the field of peripheral vascular diseases, and this volume accurately reflects the extent of knowledge and interest of the average cardiologist.

There are chapters upon all the conventional aspects of heart disease, and the author's classifications with reference to etiology, functional state, and anatomic changes are those now generally approved by most authorities. His discussion of etiologic factors such as rheumatic fever, syphilis, and hypertension is very sound, and seems to include all important recent contributions with the single exception of the surgical treatment of hypertension, which he probably regards as still of unproved value. The chapters dealing with congestive heart failure, anginal heart failure (here designated "failure of the coronary circulation"), failure of the peripheral circulation, and the treatment of these conditions, are among the best in the book, and are worthy of praise. There is a long chapter dealing with the cardiovascular system in anemia, chronic pulmonary disease, chronic renal disease, minor infections, anesthesia, pregnancy, and athletics, and it would be well if all practitioners could be thoroughly familiar with the sane comments contained therein.

Obviously, the author has aimed at presenting in rather brief and authoritative form the most important aspects of current knowledge in this field, in so far as these are useful in the diagnosis of disease and treatment of patients by the practitioner. He has succeeded extraordinarily well. One is constantly impressed by his wide knowledge of recent literature, his ability to summarize broad topics in a few sentences, and especially by his sane judgment, which is obviously based on extensive experience. There are very few statements in the book to which one can take exception, and these are of minor importance. It is a pleasure to commend it without reservation.

H. M. MARVIN.

RHEUMATISCHE KREISLAUFSCHÄDIGUNGEN: By Oberarzt Dozent Dr. Siegfried Dietrich, II Med. Univ.-Klinik Berlin, with a foreword by Professor Dr. G. von Bergmann. 178 pages, 34 illustrations, 1938, Theodor Steinkopff, Dresden and Leipzig.

This is volume 7 of the system called *Der Rheumatismus*, edited by Professor Dr. Rudolf Jürgens. The monographs cover the entire field of rheumatic diseases. Dr. Jürgens explains in the editor's foreword the widespread prevalence and importance of the rheumatic diseases, the lack of understanding of their nature, and his ambitious and basically sound plan of bringing together all of the facts and newer contributions of investigators and teachers and the experiences of specially interested physicians. He aimed to include every important item that in any way might help in the solution of any of the many problems of rheumatism in all of its forms and hoped to treat thoroughly the recognition, pathogenesis, prophylaxis, pathology, clinical manifestations, and management and treatment of each type of rheumatic disease. Besides a consideration of pharmacologic agents, the natural

methods of healing, physical therapy, including helio-, electro-, hydro-, and balneotherapy, gymnastics, massage, and climatic management, discussions by eminent physicians and investigators were to be emphasized. It was planned to make each monograph complete in itself.

In a foreword to this volume, Prof. Dr. G. von Bergmann points out that Dietrich's monograph is the outgrowth of the traditional interest of the members of his clinic in the whole subject, to the practical knowledge of which many contributions had been made by his predecessors. He points out that the newer conceptions of the German rheumatism clinic which are set forth by Dietrich are most significant.

Dietrich's monograph fulfills the editor's expectations. He separates rheumatic fever from infectious arthritis and agrees with the English and American workers that the carditis should be regarded as the chief manifestation of the disease, while the polyarthritis, chorea, and other symptoms are complications. Dietrich states that fresh rheumatic pancarditis or acute inflammatory rheumatism may be the first act of the tragedy, which is rarely completed in a single act, and usually returns in the form of carditis. The seriousness of this situation is duly emphasized as a problem of social medicine, since two-thirds of the afflicted persons, most of whom are youths, succumb or become total invalids within fifteen years. In Germany every fourth death is due to heart disease, and 31 per cent of all invalided males were suffering from disease of the circulatory system. The social welfare attitude that the author emphasizes seems justified. The work of the English and our own New England group of workers has been substantiated. The author has a thorough knowledge of the literature and has had broad clinical experience. His contribution is worthy of study and should be a source of much help and some encouragement to those working in this important field. He hopes that prophylaxis by increasing resistance to infection will decrease the destruction that is being wrought by rheumatic fever.

GEORGE HERRMANN.

ELEMENTS DE PHYSIOLOGIE CLINIQUE DE L'APPAREIL CIRCULATOIRE (Essentials of Clinical Physiology of the Circulatory Apparatus): By J. Castaigne and P. Dodel. Masson et Cie, Paris, 1939, 143 pages, 81 illustrations, price 27 fr.

A pocket-size book giving the information on the circulation found in most textbooks of physiology, with special emphasis on its clinical importance and relationships.

ISAAC STARR.

DIE PERIPHEREN DURCHBLUTUNGSSTÖRUNGEN (MEDIZINISCHE PRAXIS, BAND 27): By Dr. med. habil. M. Ratschow, Dozent für innere Medizin a. d. Martin-Luther-Universität Halle, a. S. 193 pages, 46 illustrations, 1939, Theodor Steinkopff, Dresden and Leipzig.

The purpose of this twenty-seventh monograph of the series of Medical Reviews entitled "Medizinische Praxis" is, according to the introduction by Cobet, to fill the gap in the German literature which was filled in the English by Sir Thomas Lewis' book on peripheral vessels, and to collect and interpret in German those facts learned about the peripheral circulation during the last ten years which have a clinical bearing.

The introduction (six pages) limits "peripheral disturbances in blood flow" to local phenomena, as opposed to cardiac failure. Thus the role of the minute vessels in local allergy, but not in anaphylactic or traumatic shock, comes in for discussion. A historical note, perhaps necessarily brief and incomplete, follows. The

next section (ten pages), entitled "Structure, Function, and Interplay of the Peripheral Vessels," is devoted almost entirely to function. The description is formal, and so brief as to be useful only in outlining the methods of vascular regulation for beginning students.

A discussion of the general characteristics of, and tests for, peripheral vascular disturbance occupies the next forty pages. Pain on exercise he believes is the "cry of the tissues for oxygen." He does not discuss Lewis' work concerning a special substance as a cause of pain, but cites Brown and Allen as having shown, by novocainization, that arterial spasm can interfere markedly with local circulation. Rest pain is more complicated; besides marked reduction of the circulation, he believes neuritis may be a frequent cause, and that it may be distinguished from pain due to "prenecrotic states" by failure to relieve it by increasing venous pressure. In describing a work test for pain, the interesting fact is brought out that by elevating the leg a difference between the old and the young as regards appearance of pain can be demonstrated.

There follows a short discussion of the physiologic significance of color changes in the skin with changes in environmental temperature and position. Considerable space is devoted to the meaning of surface temperature and its measurement. Discussing only well-known facts, he points out that normal surface temperature may occur in the presence of well-marked narrowing of large arteries, and, therefore, advocates the usual tests of function by direct and reflex heating or cooling of the region to be tested, and by nerve block combined with temperature measurements to distinguish functional from organic arterial disease. Only a passing statement is made concerning oscillometry and plethysmography, which methods, he says, in Germany are relegated solely to "scientific" use, but appear to have been used clinically to advantage in America.

Reactive hyperemia, which he places under the heading, "Disturbances of the Ability of the Peripheral Vessels to Dilate," is adequately treated. He leans to the view that reactive hyperemia is, as Lewis believes, probably due to the liberation in the tissues of more than one substance, and in so doing he embraces the notion of O. Muller that it may in part be the result of nervous influences. His apparatus for interrupting arterial circulation is described in detail, and he finds that study of reactive hyperemia is useful in distinguishing between certain vascular disorders, as follows:

1. *Delayed* appearance with *diffuse* development of *full* color means complete occlusion of a large artery with good collateral circulation.

2. *Delayed* appearance with *diffuse faint* color means that narrowing of the finer vessels (arteriosclerosis, for example) is present.

3. *Delayed* appearance with *marked mottling* is indicative of very severe curtailment of the blood supply and is usually seen in endarteritis obliterans.

4. *Prompt* appearance with *good* color which disappears *quickly* suggests the angiospastic diseases (Raynaud's).

5. *Prompt* appearance with *deep* color which disappears very *slowly* suggests acrocyanosis.

The next chapter (fourteen pages) is given over to direct methods for study of vessels, of which there seem to be two, namely, capillary microscopy and angiography (roentgenography of arteries and veins after injection of contrast media). For estimation of the circulation he recommends capillary counts and F. Lange's test, namely, the time required for the flow of blood in the capillaries to cease after occlusion of the circulation.

The discussion of angiography is full and interesting. The author makes several points: (1) the extent of collateral circulation can be accurately ascertained. (2) If the shadow of the lumen of a vessel ends in a point, the oc-

clusion is probably spastic; if blunt and transverse, probably organic in nature. (3) Corkscrew course and irregular width of lumen suggest arteriosclerosis; straight course and diffuse narrowing suggest endarteritis. (4) In prognosis of the life of an extremity, radiographic measurement of the length of time necessary for the veins to empty after arterial injection is important. (5) Valuable information may be obtained as to whether varices are due to obstruction of the deep veins or to failure of the valves of the communicating veins. Many reproductions of good roentgenograms accompany the text and illustrate these points. As a contrast medium the author prefers thorotrast (thorium dioxide) to the iodine-containing compounds such as Uroselectan, because the injection is unaccompanied by pain, and because he believes that the basic studies of von Lohr and the experiences of "the whole world" have now shown that the complications which follow its use are "trifling." His procedure is to shut off arterial circulation for five minutes prior to injection, in order to dilate the finer arterioles, and then to follow the course of the material after injection by serial roentgenograms.

The next section, a long one, is headed "Diseases Depending upon Disturbance of Blood Flow" (pages 73-136). A lengthy discussion concerning the nature and possible varieties of disturbance of flow enables the author to discard most of the older names for peripheral vascular diseases in his classification, and to set down simply several sorts of reaction. He concludes that "anders artige Reaktion Bereitschaft" means simply that subliminal stimuli take on vasomotor roles under certain circumstances.

His classification divides diseases into four main headings: (1) *Angiopathies*, or diseases resulting from an increased tendency of arteries either to constrict or to dilate, or to do both. In this category fall Raynaud's disease, ergotism, and erythromelalgia. (2) *Angiitides*, which include endarteritis obliterans, infectious arteritis, mechanical (physical) arteritis, such as frostbite, and phlebitis. (3) *Angioses*, i.e., degenerative lesions which include diabetic and senile arteriosclerosis and varicose veins. (4) *Occlusions* of arteries of any sort. External and internal causes of disturbances of the peripheral circulation are then briefly mentioned, namely, cold and moisture, nicotine, infections and endocrine disturbances (the list seems incomplete), and several pages of description of pathologic changes which take place in the arterial walls and tissue follow. Numerous good photomicrographs of various thrombotic processes are reproduced. Various diseases of the peripheral circulation are then described briefly under the headings given in this classification.

A short section is devoted to main points in diagnosis on a basis of signs and behavior with respect to the various functional tests, and a brief summary of how to localize occlusions from the character and site of pain is presented.

The next twenty-five pages (144 to 169) deal with treatment. After stating the aims of treatment, he sums up the general rules in seven "commandments": (1) Keep the extremities warm, (2) avoid injury and don't cut your own corns, (3) don't wear circular rubber garters, (4) don't cross your legs, (5) drink plenty of coffee and water, (6) avoid rich meats, and (7) don't smoke. The author recommends many of the usual forms of therapy, such as local and general heat, diathermy, nerve block, and reactive hyperemia. He tends to believe that just as good an effect on the circulation, if not a better, can be obtained from intermittent occlusion of the veins as from the various suction and pressure apparatuses. Nitrites, euphyllin, eupaverin, strychnine, and, especially, various preparations of theophyllin are useful. He finds that the various choline derivatives, acetyl-β-methylcholine chloride and carbaminoylcholin, have little effect, which is what he would expect from the rapidity of their destruction in the

body. Although he believes that it is too early to make categorical statements about the use of sex hormones, he feels sure that progynon has been beneficial in women and "testoviron," though less well tested, in man. He makes the statement that progynon can be used only in women, testoviron only in men.

In the treatment of necrosis and gangrene he puts bed rest first. Next comes treatment with warm carbon dioxide baths locally, as outlined by Cobet. Considerable space and emphasis are given to the use and good effects of this procedure in necrotic lesions. Of interest, too, is the emphasis which he puts upon the use of local infiltration of tissues with a solution of acetylcholine and 1 per cent novocaine solution. The extraordinary relief from pain obtained in this way is, to the author, very important, since it makes the use of narcotics unnecessary for hours at a time. He believes that the circulation to the tissues is also considerably enhanced by the presence of these drugs. The last step in treatment is the resort to surgery, and the indication for it is principally a rapid increase in the size of the gangrenous area under conservative treatment. Intra-arterial injection of contrast media to determine the site of amputation is a necessary preliminary.

The section on prognosis takes but half a page; it says little more than that most of the diseases under discussion are chronic, and that the prognosis is, in general, bad.

The monograph closes with eight pages devoted to the importance of testimony in connection with accident and invalid insurance. He notes the frequency with which the onset of symptoms follows an accident, but closes with a warning that, since even Raynaud's disease can be fatal, deflection of judgment in the clear distinction between accident and disease is not permissible.

It is a useful monograph but can hardly replace Sir Thomas Lewis' book.

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